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Volume 247 DECEMBER 18, 1952 Number 25

POLYPS OF THE RECTUM AND COLON AND THEIR RELATION TO CANCER*

CLAUDE E. WELCH, M.D.,† JOHN B. MCKITTRICK, M.D.,‡ AND GLENN BEHRINGER, M.D.§

BOSTON

POLYPS of the rectum and colon have been observed with increasing frequency in the past few years, particularly because of the emphasis placed upon sigmoidoscopy as a method of early detection of cancer. The surprisingly high incidence of microscopic carcinoma in such polyps has raised many questions in the minds of surgeons who must deal with these problems. In an attempt to clarify the relation of polyps to cancer, we have accordingly, in the past few years, co-ordinated our clinical studies with the departments of pathology of the Massachusetts General Hospital. The conclusions presented here must be regarded as a codification of our present concepts, which may be modified as this study is continued.

It is impossible to present briefly many interesting aspects of the nature and therapy of polyps. Pertinent papers, particularly those dealing with pathological studies, are numerous enough to make any student regard most of his contributions as merely confirming what has been said more effectively in the past. We should prefer, therefore, not to discuss many conclusions that have been accepted but to consider one problem alone: that of the surgeon who is faced with a single or a few adjacent polyps of the large bowel.

Twenty years ago, the clinical solution was easy — namely, to destroy the small polyps by electrocoagulation or excision, perform bowel resections for large polyps and neglect the microscopical reports. Unfortunately, this tendency still persists in many quarters. A slightly more accurate teaching is that all polyps can be divided into two groups — the adenomatous polyps and the papillary adenomas. Adenomatous polyps, even though microscopically malignant, are supposed to be clinically benign so that cancer control may be achieved by local removal of the polyp. Papillary adenomas, even if microscopically benign, are clinically malignant; they tend to recur locally and to degenerate into cancer so that segmental resection of the involved bowel and mesentery should be carried out.

To clarify the problem we have studied cases diagnosed as polyps in the Massachusetts General Hospital from 1937 to 1952. At present, the diagnosis of adenomatous polyp is made in approximately 100 cases a year. However, it is apparent that for purposes of the present discussion, many of these polyps should not be included.

Excluded from consideration are the following groups of cases:

Adenomatous polyps associated with a distinct typical carcinoma. Such adenomas are extremely common, occurring with about 20 per cent of all cancers of the colon and rectum, and are usually located near the cancer. Often, an adenomatous polyp in the rectum is a signpost directing attention to the full-blown cancer in a higher level of bowel. Such cases are not included since the therapy and prognosis will be those of the cancer.

Cancer that grossly appears sessile and ulcerated but that microscopically presents evidence that it has arisen from a polyp. According to Swinton and Warren,[1] and to Bacon, Laurens and Peale,[2] 15 per cent of all cancers of the colon and rectum show such microscopical characteristics. To the surgeon, however, these lesions are typical cancer, and therapy is not predicated on the belief that he is dealing with a single polyp.

Diffuse (familial) polyposis. The necessity for total colectomy in this disease to prevent death from cancer is well recognized.

Multiple polyps, provided that far different segments of the bowel are involved. For example, polyposis involving the transverse colon and sigmoid raises problems of therapy too extensive to be covered here.

Pseudopolyps, associated with inflammatory lesions. Ulcerative colitis is usually the underlying disease though pseudopolyps have been observed with diverticulitis and amebiasis. Occasionally, these polyps may appear within range of the sigmoidoscope, and the causative disease may fail to be appreciated. The frequency with

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which cancer develops in the colon involved by ulcerative colitis and pseudopolyposis has frequently been stressed.

Fibrous polyps, associated with hemorrhoids. They are common, but of no significance from the point of view of cancer control.

Other benign tumors of the rectum or colon, such as fibromas and the so-called benign lymphomas. Though grossly polypoid, they are not precancerous.

Exclusion of these cases leaves a sizable group of tumors that either are proved to be benign polyps by the pathologist or are excised by the surgeon who believes they are benign, the pathologist finding microscopical evidence of cancer. We wish to emphasize the fact that this paper deals with this restricted group — only cancers in which the gross appearance was consistent with an adenomatous polyp or papillary adenoma are included.

From 1937 to 1952 322 patients with such lesions have been observed in the Massachusetts General Hospital (Table 1). This paper presents the data

TABLE 1. *Incidence of Cancer in Polyps (Massachusetts General Hospital, 1937–1952).*

Type of Tumor	Total No. of Cases	Cases of Cancer
Papillary adenomas	27	6 (22%)
Adenomatous polyps:		
Sessile	66	14 (21%)
Pedunculated or indeterminate	229	40 (17%)
Totals	322	60 (18%)

derived from a study of these patients. Follow-up studies are based on the series of 165 cases seen in the Massachusetts General Hospital between 1937 and 1947; in this group, at least five years have elapsed after treatment. Of the 40 patients with cancer in polyps seen through the year 1947, 33 have been followed for five years or until death, and 3 for two years without evidence of recurrence and 4 have been lost.

Gross Description

The differentiation of various types of polyps is commonly made on the gross appearance. Although it is popularly believed that they may be called either pedunculated or sessile, actually it is much more important to consider them as either adenomatous polyps or papillary adenomas, since these groups vary significantly in their cancer potential.

Adenomatous polyps appear first as tiny, slightly elevated nodules on the mucosa, 2 or 3 mm. in diameter. When seen through the sigmoidoscope, such mucosal excrescences — or sessile mammillations, as they have been called — are grossly indistinguishable from physiologic changes in the normal colon or from tiny carcinomas. Fortunately, true carcinomas of this type are extremely rare, though such a case was recently reported by Weingarten and Turrell.[3] Their patient had a 2.5-mm. mucosal excrescence of the rectum that had been observed to be of similar size six years before. These sessile mammillations should always be biopsied and destroyed by electrocoagulation.

The pattern of growth of adenomas has been described by Helwig,[4] who found such lesions in 7 per cent of 1460 consecutive autopsies. Proliferation of submucosal glands occurs so that the nodule gradually becomes elevated. Later, a pedicle appears, over which the adenoma frequently hangs like an umbrella. Consequently, the pedicle may be difficult or impossible to detect (except on careful dissection). Thus adenomas assume a variety of forms — long and thin, short and fat, pedunculated, pseudopedunculated and sessile.

The presence or absence of a true pedicle is important to the surgeon. He is under a handicap, particularly when a large polyp may completely fill the lumen of the sigmoidoscope, and considerable manipulation or destruction of the polyp will be necessary before the pedicle is exposed. Occasionally, a polyp is removed, and the surgeon has no clear idea of the pedicle. The important feature is that biopsies must be taken from all levels of the polyp if it is to be destroyed by electrocoagulation. Carcinoma may develop in the tip, center or base of any of these polyps, as Helwig[4] has shown, so that adequate tissue must be given to the pathologist.

A long pedicle is encountered much more frequently with polyps of the colon, probably because of the increased peristaltic pull on the polyp in this location in comparison with the rectum. This pedicle is commonly a strip of mucous membrane, but it may be a thick fibrous stalk. The distinction between the two may be difficult for both surgeon and pathologist. For example, 1 polyp in this series was described by the surgeon as arising from a pedicle 15 cm. in length. To the pathologist, this polyp had a short pedicle and was attached to a strip of mucous membrane 10 cm. long. We have observed that any surgeon who wishes to produce a pedicle on a polyp of the colon need only make the appropriate amount of traction to tent up the mucous membrane a sufficient distance.

Much of the confusion about polyps arises from this feature alone. Dr. Benjamin Castleman, in the Pathological Laboratory of the Massachusetts General Hospital, states that he has never seen metastases from a cancer arising in a polyp of the colon with a long stalk. However, he often rejects cases in which the surgeon has been convinced that he was dealing with a long pedicle. This divergence of views may be illustrated by the following case.

Case 1. P. P. (M. G. H. 446667), a 72-year-old woman, had a sigmoid polyp for which laparotomy was carried out. At operation, a colotomy was done, and a polyp with what the surgeon called a "long pedicle" excised. The specimen was immediately examined, frozen section being reported negative for cancer. Final sections showed adenocarcinoma, Grade III. Nothing further was done surgically because of the patient's age. Three years later she re-entered the hospital with recurrent rectal bleeding, a mass of cancer in the left lower quadrant and metastases in the liver. Review of the microscopical sections showed what Dr. Castleman interpreted as a polypoid carcinoma arising in a pedicle of mucous membrane and not in a true stalk.

This distinction between pedunculated and sessile polyps seems to have been greatly overemphasized. We believe the presence of a pedicle should not be the determining factor in the selection of operation for several reasons. In the first place, the surgeon and pathologist are often in serious disagreement about the presence of a pedicle. Secondly, the gross and microscopical differentiation of tented mucous membrane and a true stalk is difficult or impossible in many cases. Finally, true stalks contain lymphatics and blood vessels just as normal mucous membrane does, so that, theoretically, metastases can occur in either. We have encountered metastases in 3 cases in which the surgeon was convinced that he was dealing with a benign polyp with a true pedicle. Klein and Scarborough[5, 6] have presented evidence of lymph-node metastasis from pedunculated polyps of the colon. We agree with them that the presence of cancer in such a polyp is much more important than the presence of a pedicle. A long pedicle is good insurance against local recurrence but does not guarantee freedom from metastasis.

The *papillary adenomas* constitute about 15 per cent of all rectal polyps. They are soft and velvety, usually with innumerable fine papillary folds, and tend to involve a wide area of the bowel. They extend laterally by proliferation of the epithelium, so that a wide area of rectum may be involved. Polypoid projections may occur but arise from a plateau of tumor rather than from normal mucous membrane. They are usually single, tend to recur after attempts at local removal and later frequently degenerate into cancer. The differentiation of this type of polyp from the single adenomatous polyp is often easier on gross than on microscopical examination.

Although the differentiation of small polyps into adenomatous polyps and papillary adenomas may be impossible, we agree with Sunderland and Binkley[7] that it is essential to differentiate the well marked cases. These authors have recently emphasized the significance of the papillary adenoma, finding that 68.7 per cent of the patients in their series had cytologic areas of cancer, whereas invasive carcinoma developed in 39.5 per cent.

In the Massachusetts General Hospital series of 322 polyps, 26 were typical papillary adenomas. All were in the rectum or low sigmoid; 12 per cent of the rectal polyps were of this type. A radical attack was instituted on all of them unless some contraindication prevented it. Local removal was attempted in only 5 cases; of these, cancer from which the patients died developed in 2, and in another an independent cancer of the rectum developed just above the papillary adenoma. Of all 26 cases, there was microscopical evidence of cancer in 7, with 3 deaths from carcinoma. The incidence of cancer — approximately 22 per cent — would have been much higher if radical resections had not been employed at an early time after discovery of the polyp.

Microscopical Description

These polyps have been divided microscopically into several groups (Table 2). The benign adenomatous polyp shows well developed glands with no unusual cellular features. The atypical adenomatous polyp exhibits a moderate degree of abnormality evidenced by loss of polarity of cells, hyperchromatism of nuclei and so forth. The "carcinoma in situ" shows no invasion of the basement membrane, but the cellular characteristics are otherwise typical of cancer. Carcinomas are nearly always adenomatous, though 1 case of a typical colloid carcinoma in a pedunculated polyp was encountered. When the entire group of 322 polyps is considered, 262 were benign, and 18 were associated with carcinoma in situ, 18 with adenocarcinoma, Grade I, and 22 with carcinoma, Grade II, and 1 each had carcinoma, Grade III, or colloid cancer. Thus, cancer was present in 18 per cent of the cases, approximately a third being carcinoma in situ, a third adenocarcinoma, Grade I, and a third high grades of cancer.

Table 2. *Pathological Reports and Metastasis.*

Pathological Report	Total No. of Cases	Cases of Metastasis*
Carcinoma in situ	18	0
Adenocarcinoma, Grade I	18	1
Adenocarcinoma, Grade II	22	7
Adenocarcinoma, Grade III	1	1
Colloid carcinoma	1	0
Totals	60	9

*Proved by resection or death from cancer.

Table 3. *Incidence of Cancer in Polyps of the Rectum and Colon.*

Location	Total No. of Polyps	Total Polyps with Cancer
Rectum	220	36 (16.6%)
Colon	102	24 (23.6%)
Totals	322	60 (18.6%)

When the polyps of the rectum and colon are considered separately, the evidence of carcinoma is, respectively, 17 and 23 per cent (Table 3). There

is no significant variation in the distribution of the different microscopical types of cancer. The lower incidence of cancer in rectal polyps is due to the fact that many small polyps can be detected and treated through the sigmoidoscope whereas polyps of a similar size in the colon could not be visualized on barium-enema examination.

Prognosis

A study of the follow-up results indicates that the microscopical diagnosis is important so far as the prognosis is concerned. We have encountered no evidence of recurrence in the patients with adenomatous polyps completely removed by local operations, though local recurrence or persistence was noted in several cases of papillary adenomas. The so-called "atypical polyps" behaved no differently. Patients with carcinoma in situ also all did well, indicating that this diagnosis can be regarded with less caution in the colon than in the stomach. Two patients with adenocarcinoma, Grade I, showed invasion of the pedicle, though only 1 had evidence of metastasis to the regional lymph nodes; this tumor was a papillary adenoma.

However, with the higher grades of malignancy, the prognosis was much worse. Of the 24 patients with adenocarcinoma, Grade II or III, or colloid carcinoma, arising in a polyp, 6 are known to have died of this cancer.

The importance of repeated follow-up visits for patients with polyps has been stressed by all observers. We found as well that, despite a somewhat haphazard policy, the known incidence of later polyps and cancer of the large bowel was very high.

Morbidity and Mortality

It is necessary to recount the complications encountered in the surgery of these polyps since the choice of operation is, to some extent, dependent upon this factor (Table 4).

Table 4. *Mortality in Polyps of the Rectum and Colon.*

Surgical Procedure	No. of Cases	Hospital Deaths	Late Deaths From Cancer
Polypectomy:			
Rectum	183	0	6
Colon	64	0	1
Radical resection:			
Rectum	37	1*	0
Colon	38	1†	0
Totals	322	2	7

*Death 2 months after resection of papillary adenoma of the rectum.
†Resection for obstructing diverticulitis and incidental polyp.

Rectal Polyps

Local excision of the polyp through the dilated rectum in 1 case led to a severe submucosal hemorrhage that dissected far up the sigmoid and required combined abdominoperineal resection. Electrocoagulation through the sigmoidoscope led to severe intraluminal hemorrhage in several cases. Control was occasionally obtained by grasping of the bleeding pedicle with a biopsy forceps and applying the coagulating current to the forceps. Gelfoam aided in others. Perforation was observed in 1 case; immediate laparotomy, suture of the perforation and polypectomy were carried out, without further complications.

Polyps of the Colon

In this group, there were 2 hospital deaths. One patient died of peritonitis after a resection of the sigmoid for diverticulitis and incidental polyp. The other died two months after a resection and anastomosis for a large papillary adenoma of the intraperitoneal portion of the rectum from pyelonephritis. The other complications followed polypectomy. In 1 patient a pelvic abscess requiring a permanent colostomy developed; he never recovered completely and died two years afterward of carcinoma arising in the ascending colon. In another patient pelvic cellulitis occurred after colotomy; 1 had a hemorrhage, and still another a sharp angulation of the bowel at the site of colotomy. One patient had a polypectomy, and on his first visit to the outpatient department a month later, another polyp was demonstrated a few centimeters lower in the bowel; this required a second laparotomy.

Therapy

A complete discussion of the methods of therapy employed for the removal of these polyps and the technical considerations is beyond the scope of this paper. Only the details that are related to cancer control are noted. Papillary adenomas and adenomatous polyps must be considered separately.

Papillary Adenomas

When the diagnosis of papillary adenoma is established by gross inspection and biopsy, radical resection should be carried out. Nearly all these lesions are located in the rectum, often so near the sphincter that an anastomosis cannot be performed. However, if the tumor is soft throughout and biopsies are adequate and indicative of benign polyp only, there is no reason why resection and anastomosis should not be carried out if they are technically feasible.

Adenomatous Polyps

In general terms, adenomatous polyps are located either in the colon, where laparotomy is necessary for excision, or in the rectum, where removal through the sigmoidoscope or excision through the anus is possible. Some polyps of the sigmoid can be removed through the sigmoidoscope; our only rule is that adequate visualization of the entire polyp must be possible through the sigmoidoscope. In this series 2 per cent of cases occurred in the

ascending, 2 per cent in the transverse, and 3 per cent in the descending colon, and 20 per cent in the middle or upper sigmoid. The remainder (73 per cent) were accessible through the sigmoidoscope.

When located in the rectum, some of the polyps can be withdrawn through the anus and excised in toto with a base of normal mucous membrane. This has proved satisfactory since a total biopsy can be obtained. We have had no experience with local excision after posterior proctotomy as advocated by some surgeons. Other polyps are removed by biopsy forceps, electrocoagulation or snare, depending on their size and location.

In all these cases, if the microscopical report is benign polyp, carcinoma in situ or adenocarcinoma, Grade I, we are satisfied with complete destruction of the polyp with its base, and adequate follow-up study. There is no evidence from our data that more radical operations are necessary. In the polyps that demonstrate higher grades of cancer, we believe that radical resection is wise, as a general rule. In a certain group of cases, the sphincter can be preserved either by a pull-through procedure or by an anastomosis performed through the perineum.

Polyps of the Colon

Although colotomy and polypectomy is the usually accepted operation for polyps located above the reach of the sigmoidoscope or low in the sigmoid, but too large to be treated safely by electrocoagulation, we believe it is better to carry out a segmental resection of the colon. However, if such a principle is to be accepted, it is essential that the individual surgeon examine his morbidity and mortality rates carefully. If they are high, the simpler operation of polypectomy should be chosen when possible. But if, as in this hospital, the rates are closely comparable for polypectomy and resection, the arguments in favor of resection should be considered. These reasons, all of which will result in better cancer control, are as follows:

In the first place, the possibility of local recurrence is eliminated. In this series, 102 patients with polyps of the colon had operations; 24 patients had cancer; 7 were carcinoma in situ, 7 adenocarcinoma, Grade I (with invasion of the pedicle in 2), 8 adenocarcinoma, Grade II, 1 adenocarcinoma, Grade III, and 1 colloid carcinoma. It is certain that the possibility of local recurrence after simple polypectomy is high in this group. As pointed out below, in the entire rectum and colon, 9 local recurrences have been noted after 34 local excisions of carcinomatous polyps.

This local recurrence may be noted rarely even if the original pathological report is benign adenomatous polyp. Castro, Ault and Smith[8] have described 2 such cases. Fortunately, in our group, only 2 similar cases have been encountered; both were in the rectum, where they were discovered quickly by palpation and proctoscopy.

If local recurrence develops after polypectomy and the base of the polyp is above reach of the sigmoidoscope, the only way it can be detected is by barium-enema examination — a cumbersome method that cannot be relied upon until the recurrence is relatively extensive.

Secondly, lymph-node metastasis, if present, is adequately treated. This involves a consideration of the frequency of metastasis from these carcinomas. Metastasis is comparatively rare. Out of 26 radical resections for these carcinomatous polyps, only 2 patients had lymph-node metastases, and these were both in the pericolic nodes. It thus appears that a somewhat less radical operation is necessary for a carcinomatous polyp than would be required for the usual cancer of the colon. Obviously, in the rare cases in which positive lymph nodes are recognized at operation, a more extensive resection is carried out.

Thirdly, additional polyps are often discovered in the resected specimen. This is particularly true in the ascending colon, possibly because radiologic diagnosis is less accurate in that section of the bowel, or because a wider segment of bowel is usually resected. In this series, there were 27 benign polyps that were removed by resection of the bowel when polypectomy would have been feasible. One or more additional polyps were found in 10 cases, with an average of 1.8 polyps present in each specimen.

Finally, in certain cases, the technical procedure of resection and anastomosis will be easier than that of polypectomy. This is particularly true when the sigmoid has been deformed by diverticulitis.

These considerations may be applied to the present series of 102 colonic polyps to determine the proper operation. It may be assumed that all surgeons would prefer segmental resection for the papillary adenomas (12 cases). Also, the sessile adenomatous polyps demand segmental resection (13 cases). In addition, most surgeons would, if they could identify them, do such a resection for pedunculated polyps that contain cancer (16 cases). Finally, 8 patients had diverticulitis as well, requiring resection. Thus, there is fairly general agreement that nearly half the colonic polyps should be treated by segmental resection.

If the surgeon restricts polypectomy to polyps with long, fibrous pedicles and resects all others, he will make few mistakes. However, we prefer to eliminate the hesitancies and uncertainties of polypectomy and consider segmental resection the standard procedure for all polyps.

An adequate operation can, of course, be done in other ways. Many surgeons prefer the simpler

operation of colotomy and polypectomy whenever possible, and we agree that in certain cases, in which a short operation in an old patient is necessary, such a technic is better. But the surgeon who employs polypectomy as a routine procedure must prepare for other possibilities. If he opens the bowel and finds a sessile polyp, he should resect. He must depend upon frozen sections as a guide in all questionable cases; this is satisfactory in some institutions, but we have not been convinced that it is dependable. The surgeon must look for other neighboring polyps in addition to the obvious one. Finally, he will surely be faced with the necessity of a second laparotomy in certain cases in which the final microscopical sections prove that he was too conservative in the selection of his original operation.

We have found that some break in this routine is the rule, particularly when the pathological sections indicate that the original operation has been too timidly conceived. It is a rare case in which the surgeon has reoperated, even when the pathological evidence has indicated that he should do so.

However, either of these two methods — polypectomy, with early reoperation when necessary, or resection for all polyps of the colon — is adequate for cancer control. The selection is a matter of choice for the individual surgeon.

Discussion

Other interesting questions arise in the discussion of the treatment of polyps. Several merit further discussion.

Effect of Local Excision

What is the fate of patients with polyps of the rectum or colon that, on microscopical examination, are shown to contain cancer, provided that the lesion is treated only by local excision? This important question is difficult to answer from the literature. A collection from various sources is shown in Table 5. It will be noted that there is considerable variation in these reports. Undoubtedly, the difference is largely accounted for by the inclusion of small but otherwise typical carcinomas, or of papillary adenomas by some authors, whereas others exclude them.

Table 5. *Results of Local Excision for Cancer Arising in Polyps of the Colon and Rectum.*

Authors	No. of Local Excisions	Cases of Metastasis or Recurrence
McLanahan et al.[9]	38	10
Klein and Scarborough[3]	36*	9
Lahey[10]	33	0
Castro, Ault and Smith[8]	21	2
Colvert and Brown[11]	14	1
Sandusky and Parsons[12]	10	0
Massachusetts General Hospital series	34	9
Totals	186	31 (17%)

*11 patients had radical resection after positive frozen section.

In this series, 34 patients had a local excision of such a carcinoma. In all cases the surgeon believed that he was dealing with a benign polyp, but cancer was found by the pathologist. Nine patients are known to have had metastases later or to have died of cancer. It is important to note that these recurrences developed in patients with papillary adenomas or those with adenomatous polyps of a high grade of malignancy.

Early Detection of Recurrence

Can recurrence in patients who have had a local excision of a carcinomatous polyp be detected early so that a radical operation can be performed if necessary? This requires consideration of the number of patients in whom lymph-node or bloodstream metastases develop in the absence of local recurrence. It is our belief that such recurrences, although theoretically possible, are rare and, in most cases, locally demonstrable. Thus, of the 9 patients with recurrences, only 1 had positive lymph nodes in the absence of local recurrence. Obviously, the series is small, and more evidence is needed.

We now believe that if a patient appears who has had a carcinomatous polyp of the rectum excised elsewhere, and sigmoidoscopy gives no evidence of recurrence, the microscopical material must be reviewed with our pathologist. If the lesion is of a low grade of malignancy (carcinoma in situ or adenocarcinoma, Grade I), we are content with careful repeated sigmoidoscopic observations. If the lesion is of high malignancy (adenocarcinoma, Grade II or III), we believe it is wisest to carry out a radical resection. This is, of course, mandatory if any local recurrence is evident. Any decision must be modified considerably by the age and general condition of the patient.

Pathological Diagnosis

Underlying this whole discussion is the mute acceptance of the pathologist's opinion. Can his diagnosis on a given polyp be accepted? Errors may result from three causes. In the first place, the pathologist may not be given an adequate or representative block of tissue. For example, in 100 consecutive resected cancers of the rectum, preoperative biopsies had shown adenomatous polyp or inflammatory changes in normal mucosa in 15. Here the responsibility for error lies with the surgeon, who failed to obtain a proper specimen. This difficulty is particularly common with the large papillary adenomas, in which cancer may be found only in the central portion of the tumor.

Secondly, adequate tissue may have been provided, but the sections had been taken from the wrong portion of the block. Most laboratories

now make numerous sections of polyps, and this error is avoided.

Thirdly, pathologists may disagree on their interpretation of a given specimen. It is disheartening to present the same slide to three eminent pathologists and to receive diagnoses, respectively, of atypical polyp, carcinoma in situ and adenocarcinoma.

It seems reasonable to conclude that it is essential for the pathologists and surgeons of the same institution to talk the same language and to cooperate closely. Otherwise, errors will occur. Final responsibility for the patient and the final diagnosis must depend upon the surgeon, who can regard the microscopical sections as important but not the only testimony in the determination of the malignancy of a lesion.

Summary and Conclusions

A review of the polyps of the rectum and colon observed in the Massachusetts General Hospital from 1937 to 1952 revealed 322 cases that were finally diagnosed by the pathologist as benign, or that the surgeon treated as benign polyps, but were found on microscopical examination to contain cancer, or in which carcinoma was later proved clinically. Microscopical evidence of cancer was present in 19 per cent of all cases.

About three fourths of polyps occur within reach of the sigmoidoscope. Polyps of the rectum should be differentiated on the basis of palpation, sigmoidoscopic appearance and biopsy as adenomatous polyps or papillary adenomas. Radical resection with or without preservation of the sphincter, depending upon the location of the lesion, is indicated for all papillary adenomas, and adenomatous polyps that show malignant changes greater than adenocarcinoma, Grade I. Polyps of the colon, it is believed, are best treated by segmental resection of the involved portion of the colon.

In addition to its own cancer potential, the benign polyp is a warning signal directing attention to other present or future polyps and cancer of the entire colon and rectum.

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A CONTROLLED CLINICAL STUDY OF THE EFFECT OF X-RAY THERAPY IN CERTAIN NONMALIGNANT DERMATOSES*

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PHILADELPHIA

ONE of the tasks of modern dermatology is the critical evaluation of all empiric remedies, old and new, particularly when their use involves significant risk to the patient.

It is only recently that the appraisal of topical medicaments has been subjected to rigorous control, and it must be heartening to the busy practitioner to know that more and more the claims to the effectiveness of the multitude of local preparations furnished him will be based on scientific method, and not on the enthusiasm of the first user.

Unfortunately, the problem of drugs orally and parenterally administered is not so easily solved, especially when the diseases for which they are recommended pursue variable courses and terminate at times spontaneously. To establish beyond doubt the value of arsenic in dermatitis herpetiformis, gold in lupus erythematosus or bismith in lichen planus, for example, would require a much more thorough, protracted and objective clinical study than has as yet appeared.

The evaluation of x-ray treatment of nonmalignant skin diseases lends itself much more readily to controlled methods of study, and it is surprising that, despite the intensive use of this modality for over fifty years, such material has not been forthcoming. Surely the recommendation of such a form of treatment merely because improvement followed the therapy is not to be considered objective thinking. The psychotherapeutic potentialities in a noisy mechanical rectifier and in the connotation of

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x-rays with power in the minds of laymen should never be underestimated, nor should one overlook

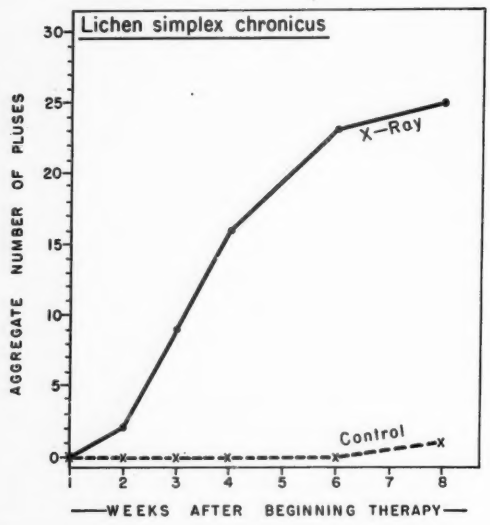

FIGURE 1. *Responses in 16 Cases of Lichen Simplex Chronicus.*

the pitfalls in interpretation of responses in non-malignant skin diseases capricious in course.

We do not regard control by comparison of results in treating and not treating symmetrical lesions as

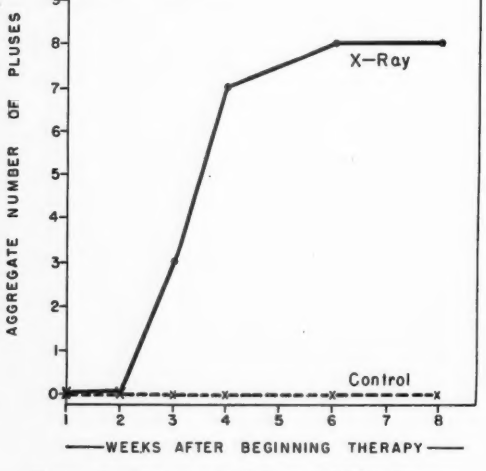

FIGURE 2. *Responses in 5 Cases of Lichen Planus.*

adequate unless the lesion is continuous from one side to the other. In clinical practice remission in a lesion on one side of the body and not on the other is often observed, even when both sides are receiving the same therapy. Moreover, in conditions in which the patient's relation to his environment is the critical feature — for example, in contact dermatitis — a preponderance of exposure on one side may well distort the results. The most serious limitation to this method, however, is that in many diseases there is either only a single lesion or symmetrical lesions so varied in size, severity or stage of evolution that comparison is meaningless.

Accordingly, in this study we have selected six dermatoses for which x-ray therapy has been recommended in the past, and have treated repre-

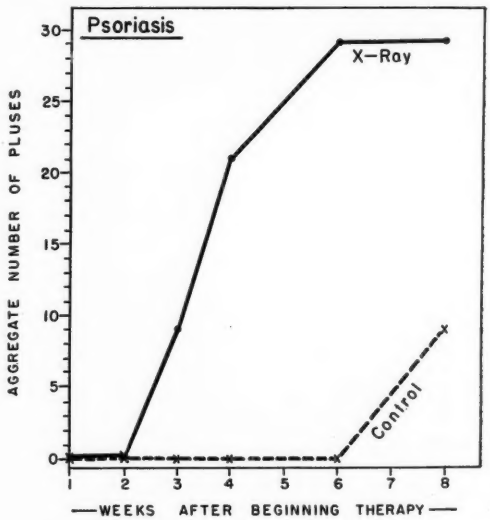

FIGURE 3. *Responses in 16 Cases of Psoriasis.*

sentative lesions in such a manner that the relative effectiveness of the therapy can clearly be determined.

METHOD

Selection of Patients

Consecutive cases of lichen simplex chronicus, lichen planus, psoriasis, nummular eczema, contact dermatitis and acne vulgaris at the clinics of the Skin and Cancer Hospital of Philadelphia were selected for treatment. Patients with a history of previous radiation were excluded.

Local Therapy

Weeping eczematous lesions were treated with wet dressings of Burow's solution (liquor aluminii acetatis) in 1:20 dilution. An ointment consisting of 10 per cent liquor carbonis detergens in hydrophilic ointment (*USP*) was applied for dry and lichenified areas. Intermediate stages were treated

with a simple wetting lotion, with or without 25 per cent olive oil depending on the dryness of the lesion. Patients with acne vulgaris received lotio alba, in addition to the usual dietary and hygienic instruction.

Administration of X-Rays

Typical diseased areas were selected. X-rays were administered to coned areas varying from 1.9 to 6 cm. in diameter, depending on the size of the lesion or group of lesions. For groups of lesions the cone was centrally placed; for solitary lesions it was eccentrically placed to avoid confusion of x-ray response with the common dermatologic phenomenon of central involution. The x-ray therapy was delivered at 90KV (HVL 0.7 mm. Al.) in doses of

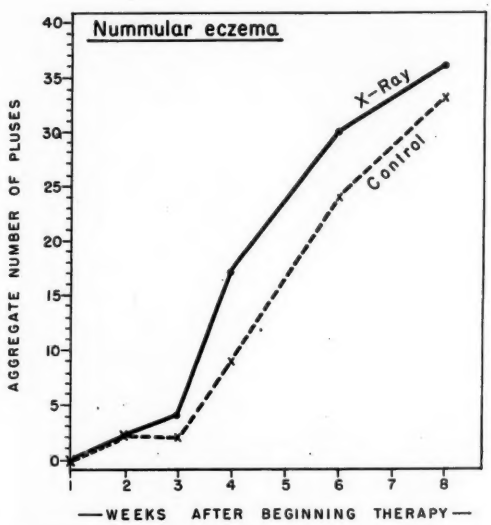

FIGURE 4. *Responses in 16 Cases of Nummular Eczema.*

100 r (measured in air) weekly for four weeks to a total of 400 r in every case, regardless of type of disease. The machine was calibrated by a physicist at the beginning and midway through the study.

Recording of Results

All patients were followed at two-week intervals for a minimum of four weeks after termination of x-ray treatment, or a total of at least eight weeks altogether. The response of the part of the lesion within the coned area, and of the rest of the lesion, which served as a control, was recorded as 1+ (perceptible involution), 2+ (marked involution) and 3+ (clinically normal skin pigmentation excepted).

OBSERVATIONS

The results of treatment are indicated in Figures 1-6. The abscissas represent weeks of therapy, and the ordinates the aggregates of response (pluses) recorded in treated and untreated areas as indicated above in the discussion of the method.

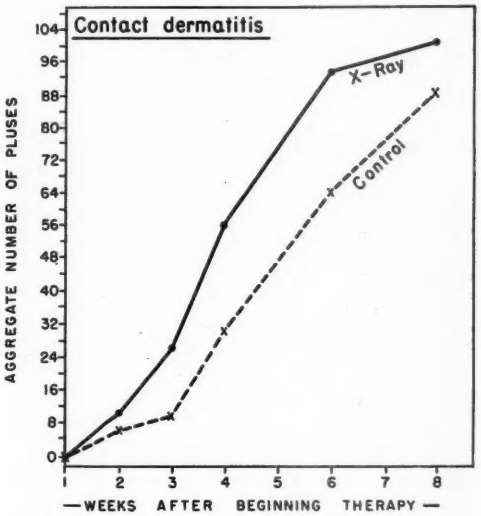

FIGURE 5. *Responses in 40 Cases of Contact Dermatitis.*

DISCUSSION

The dosage used was selected for several reasons. It was high enough to produce an effect if one was

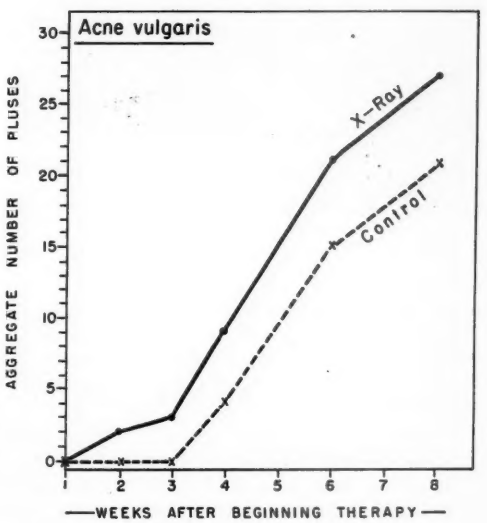

FIGURE 6. *Responses in 25 Cases of Acne Vulgaris.*

to be obtained and sufficient to do it within a period of four weeks. It was in line with, or even somewhat higher than, that prescribed by the

average dermatologist, as was the quality. Longer periods of administration were found to impair patient follow-up study to a prohibitive extent. The adequacy of the dosage for response production is borne out by the data. Follow-up examination of many of these patients for periods much longer than eight weeks showed that if involution

FIGURE 7. *Psoriasis Plaque, Inner Aspect of the Left Thigh (2.9-cm. Cone).*
A 1+ response in the radiated area occurred. The ring indicates the area covered by the x-ray cone.

within the radiated area at a rate faster than the control had not occurred by the eighth week, it was not going to; it was therefore unnecessary, for the purposes of this study, to keep the patients under observation for a longer period.

When response occurred within the coned areas at a rate different from the control, it was always clearly detectable. The borders of the circle were quite distinct, showing at times only a slight blurring or narrow transitional zone, owing, apparently, to scattered radiation from the treated area that was delivered to the skin immediately around the circumferences of the cone (Fig. 7, 8 and 9).

What was measured, then, and set up for comparison in the graphs, consisted of the rates of clearing in the radiated and nonradiated parts of the lesion. These rates were the crux of the matter, for no one will deny that all the diseases dealt with here will respond to other forms of therapy. The use of x-rays in the treatment of these diseases cannot be justified if there is no significant difference between the clearing rate in the lesions (or parts of the lesion) treated with simple topical medicaments and those given such therapy in addition to irradiation.

Inspection of the data reveals that two types of response were obtained:

The first was a consistently and significantly greater response within the radiated area than within the control. This group included cases of

FIGURE 8. *Eczematous Contact Dermatitis due to a Detergent Powder (2.9-cm. Cone).*
There was a 2+ response in the radiated area. The ring indicates the area covered by the x-ray cone.

lichen simplex chronicus, lichen planus and psoriasis (Fig. 1-3).

The second was a steady progression toward healing in both radiated and control areas, with small but discernible differences between the two. The cases of nummular eczema, contact dermatitis and acne vulgaris showed this response (Fig. 4-6).

Lichen simplex chronicus responded promptly and markedly to x-rays in the dosage and of the quality used in this study (Fig. 4). When used in the treatment of this disease, x-rays should be accompanied by whatever psychotherapeutic methods are necessary to prevent a recurrence. Retreatment in recurrent cases is attended as always by the dangers of radiation sequelae.

Lichen planus also responded promptly to x-ray therapy (Fig. 2), and in cases showing circumscribed and persistent lesions, this modality may be a valuable adjunct to therapy. More generalized varieties should at least first be given trials of other forms of therapy.

The consistent and rapid response of psoriasis to x-rays, evident from the data, is not in itself an indication for the use of such therapy in this disease. In several patients with psoriasis a prompt recurrence at the sites of radiation has been noted, and it is therefore considered dangerous to use x-rays in this benign and eminently chronic recurrent disease. The temptation to exceed safe dosages may be resisted by the physician, but not always by the patient. The "shopper" may deny previous roentgenization to achieve his goal — a quick response with little work on his part, the type of response indicated in Figure 3.

The question of the use of x-rays in the diseases of the third category is difficult. The steady progression toward healing in the control area at a rate not much slower than that in the radiated part seems to speak against the use of a potentially dangerous modality when it is not really necessary. We agree fully with the following statement of MacKee and Cipollaro*:

> The x-rays are not indicated in the majority of cases of dermatitis venenata. If the case is properly diagnosed and the cause removed the eruption as a rule will disappear quickly.

The dosage used in this study is insufficient to produce significant differences in acne vulgaris between radiated and control site. Both progressed steadily toward healing — the former at a somewhat faster rate; 400 r is by no means the dosage limit recommended in the literature. In view of the data we believe that x-rays ought to be reserved for cases of acne vulgaris found to be refractory to other forms of therapy, or cases in which it has clearly been determined that the response is not going to parallel the control curve in Figure 6.

It is not the purpose of this study to determine the permanence of results with the dosage used, but a word may be said of our experience in this matter. Two of 12 cases of lichen simplex chronicus followed for a year recurred; both were nuchal in location. One of 5 cases of lichen planus recurred in situ three months after treatment. Our observations on psoriasis have already been mentioned. Five of 16 cases of nummular eczema had recurred within six months, as is characteristic of this disease; control and irradiated sites were affected equally. There were 6 recurrences among 40 cases of contact dermatitis during the follow-up period. In 5, the control and irradiated sites were affected equally; in 1 the irradiated site was spared, although the recurrence took place two months after completion of therapy. Ten patients with acne vulgaris experienced fresh showers of lesions during a year of observation. Control and irradiated sites were affected to the same extent.

FIGURE 9. *Lichen Simplex Chronicus, Inner Aspect of the Right Thigh (5-cm. Cone).*
A 3+ response occurred in the radiated area. The ring indicates the area covered by the x-ray cone.

The management of a given case of any of the diseases studied here should, of course, be individualized. Demonstration that x-ray therapy produces a favorable response, even when the response is marked, does not necessarily constitute an indication for its use. Such evidence, however, based on controlled clinical study, is essential for the physician to have at hand in selecting properly the therapy to be used.

*MacKee, G. M., and Cipollaro, A. C. *X-Rays and Radium in the Treatment of Diseases of the Skin.* Fourth edition. 668 pp. Philadelphia: Lea & Febiger, 1946. P. 396.

Summary

A self-controlling technic for the study of the clinical effect of x-ray treatment of certain non-malignant dermatoses is outlined.

Two types of response were noted in the treatment of six dermatoses: a consistent and significantly greater response within the radiated area than within the control (cases of lichen simplex chronicus, lichen planus and psoriasis followed this pattern); and a steady progression toward healing in both radiated and control areas, with small but discernible differences between the two (cases of nummular eczema, contact dermatitis and acne vulgaris responded in this manner).

The relation of experimental results to the clinical indications for the use of x-ray in these diseases is discussed.

We are indebted to Dr. Theodore P. Eberhard, radiologist, Skin and Cancer Hospital of Philadelphia, for advice in the management of this study.

Hospital of the University of Pennsylvania

OBSERVATIONS ON THE CLOTTING DEFECT IN AMNIOTIC-FLUID EMBOLISM*

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CLEVELAND, OHIO

AMONG the rarer causes of maternal death, pulmonary embolism by amniotic fluid has been the subject of considerable recent interest.[1] In most patients with this disorder who survived the period of the delivery itself, hemorrhagic phenomena were noted before death.[2] In these women, severe uterine hemorrhage was the rule, and in a few cases, a generalized bleeding tendency was evident.[2-4] The nature of this hemorrhagic disorder has not been elucidated.

Recently, at University Hospitals of Cleveland, a patient was observed in whom profound shock occurred about thirty minutes post partum. She died eleven hours later. At autopsy, emboli of amniotic material were demonstrated in the pulmonary vessels. Approximately three and a half hours after the onset of clinical symptoms, it was noted that the patient was bleeding from the sites of venipunctures. Shortly thereafter, her blood failed to clot in vitro. Studies of the blood revealed the presence of hypofibrinogenemia, possible hypoprothrombinemia, an increase in plasma thrombin-inhibitory activity, increased plasma proteolytic activity and a slight decrease in the number of circulating platelets. These multiple defects seemed to explain the hemorrhagic phenomena observed.

Case Report

A. K. (U. H. 620-072), a 30-year-old primigravida, was admitted to the hospitals at 6:55 a.m. on November 24, 1951, in active labor. The past history was unremarkable. Her last menstrual period had begun on February 1, and the estimated date of confinement was November 8. On the evening before admission, the patient had taken 60 cc. of castor oil to induce labor. Labor began at 4:45 a.m., and 15 minutes later the membranes ruptured spontaneously. At the time of admission, the patient was apprehensive, and immediately thereafter vomited. Labor progressed rapidly. At 8 a.m. the cervix appeared to be fully dilated by rectal examination. At 8:45 satisfactory spinal anesthesia was induced with 4 mg. of Pontocaine and at 9:05, a 9-pound, normal male infant was delivered by low mid-forceps after a right mediolateral episiotomy. The placenta and membranes were delivered intact at 9:09. Pitocin, 1 cc., and ergonovine maleate, 0.2 mg., were injected intramuscularly. There was no abnormal bleeding during delivery and repair, and the mother and baby were thought to be in good condition.

At 9:30 a.m. the patient was awake; she appeared to be unusually pale. The blood pressure, which had previously ranged from 150/90 to 98/68, was unobtainable, and the radial pulse could not be felt. She was given oxygen, intravenous infusions of dextrose and physiologic saline solutions, and another intramuscular injection of 1 cc. of Pitocin. The blood pressure rose transiently to 60/50 at 10:25 a.m. but was thereafter unobtainable. The apical heart rate at this time was 120 per minute, and became more rapid and weaker thereafter. At 11 a.m. profuse vaginal bleeding, whose origin was not detected, began. The patient was given transfusions of citrated bank blood. About 1 p.m. it was noted that there were hemorrhages at the sites of venipunctures as well as from the vagina. At 2:30 p.m., a panhysterectomy was performed under local anesthesia with novocain, supplemented by nitrous oxide, oxygen and ether. There was extravasation of blood in the cervical portion of the uterus posteriorly, which extended into the left broad ligament. At operation, there was generalized oozing from all cut surfaces. Postoperatively, the patient remained in shock, and at 8:40 p.m., respirations ceased. A total of about 20 liters of fluids, including 8 liters of blood, had been administered.

At autopsy, the significant abnormalities observed were squamous cells and lanugo hairs, characteristic of amniotic-fluid embolism, in the smaller blood vessels of the lungs. The uterus was lacerated in the region of the cervix posteriorly, although the peritoneal surface was intact. Approximately 2 liters of liquid blood was present in the abdominal cavity, and there was marked extravasation of blood at the site of the abdominal incision.

Methods

Two specimens of venous blood were drawn from left antecubital veins four and a half and five hours after the recognition of shock. Part of the first specimen was mixed with dry oxalate salts in a proportion of 5 cc. of blood to 6 mg. of ammonium oxalate and 4 mg. of potassium oxalate. Plasma separated from this mixture was used for the determination of fibrinogen. The rest of the first specimen was mixed with one ninth of its volume

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of one-tenth molar solution (0.1M) of sodium oxalate, and the plasma separated from this blood was employed for all other determinations requiring plasma. The second specimen of blood was selected for the determination of the clotting time and for study of the effect of thrombin on freshly drawn blood.

The *clotting time* was determined in duplicate at room temperature in Pyrex glass tubes with an internal diameter of 11 mm. The effect of thrombin on freshly drawn blood was measured at room temperature by the addition of 1 cc. of blood to each of three tubes containing 0.1 cc. of a solution of bovine thrombin in concentrations of 10, 100 and 1000 National Institutes of Health units per cubic centimeter, respectively.*

The *concentration of fibrinogen* in the patient's plasma was determined by measurement of the tyrosine-like activity of the clot that formed when thrombin was added.[5] One hundred and fifty units of thrombin was added to 0.5 cc. of plasma, instead of the usual 50 units. The concentration of fibrinogen was also estimated by means of the tyrosine-like activity of the fraction of plasma precipitated by one-quarter saturation with ammonium sulfate. One cubic centimeter of oxalated plasma was diluted at room temperature with 2 cc. of a 0.85 per cent solution of sodium chloride and 1 cc. of a neutralized solution of ammonium sulfate, saturated at 4°C. The precipitate that formed was washed with one-quarter-saturated ammonium sulfate before its tyrosine-like activity was determined.

Prothrombin-deficient plasma was prepared by a mixture of normal oxalated plasma with a fifth of its volume of powdered barium sulfate. The mixture was incubated at 37°C. for ten minutes, and the plasma separated by centrifugation.

The *proteolytic* and *protease-inhibitory activities* of plasma were measured by methods previously described.[6] Bovine fibrin, prepared by mixing of bovine fibrinogen† and bovine thrombin,* was used as a substrate in these experiments, and the inhibitory activity of plasma was tested against bovine fibrinolysin (plasma proteolytic enzyme).* The concentration of bovine fibrinogen was 250 mg. per 100 cc., instead of 330 mg. previously employed.[6]

The *buffer solution* used throughout was 0.025 M barbital in 0.125 M sodium chloride, at pH 7.5.

Observations

Because of the collapsed state of the patient's veins, it was possible to obtain only small portions of her blood, and our studies were therefore limited. The clotting time of whole blood was determined in duplicate. Fifty-five minutes after the blood was drawn, neither sample had clotted. It was therefore evident that the hemorrhagic state had been accompanied by a defect in the clotting mechanism.

In general, venous blood may be incoagulable for one of three reasons: the blood when it is shed may lack sufficient amounts of the various elements needed for clotting; the blood may contain some substance that inhibits one of the stages of clotting; or some element needed for clotting may be destroyed in shed blood as the result of the proteolytic activity of the plasma. These various possibilities were tested.

Fifty-five minutes after the blood was drawn, a large amount of bovine thrombin (100 units in 0.1 cc. of buffer) was added to the first of the two clotting tubes. The blood in this tube clotted promptly, signifying the presence of appreciable amounts of fibrinogen at this time. The tube of clotted blood was then incubated at 37°C. Forty minutes later, the clot had lysed completely. The second tube of unclotted blood was allowed to stand at room temperature. Clotting did not occur during the eight hours after the blood was drawn. The tube was not observed during the next twenty-two hours. At the end of that time, the blood was still liquid, and it did not clot when 100 units of thrombin was added. Presumably, either the blood had clotted sometime between eight and thirty hours, and the clot had lysed, or the fibrinogen in the plasma had been destroyed before clotting could take place.

A number of demonstrable alterations in the clotting mechanism may have contributed to the phenomena that have been described. The concentration of fibrinogen in the patient's plasma was diminished. The concentration of fibrinogen was 68 mg. per 100 cc. when measured by conversion to fibrin by the addition of thrombin. This was less than a fourth of the average concentration in normal, nonpregnant women. There was no appreciable difference in the concentration of fibrinogen in a sample of plasma tested an hour after the blood was drawn and in one tested after seven hours at 4°C. To rule out the possibility that the determination was in error because the conversion of fibrinogen to fibrin was impaired, the presence of hypofibrinogenemia was confirmed by a second method. The amount of protein in the fraction of plasma precipitated by one-quarter saturation with ammonium sulfate was measured (this fraction contains virtually all the fibrinogen of plasma). By this technic, the concentration of protein in the precipitate was 61 mg. per 100 cc.

The patient's plasma inhibited the clotting action of small amounts of thrombin. This thrombin-inhibitory effect was demonstrable even when the hypofibrinogenemia was corrected by the addition of normal prothrombin-deficient plasma or bovine

*Obtained through the courtesy of Parke, Davis and Company, Detroit.
†Obtained through the courtesy of Dr. Walter Seegers, Wayne University, Detroit.

fibrinogen (Tables 1 and 2). Slight hypoprothrombinemia also appeared to be present. The clotting time of a mixture of equal parts of oxalated plasma, barium-sulfate-absorbed normal plasma, thromboplastin (CH 61)* and 0.025 M calcium chloride

TABLE 1. *Effect of Thrombin on the Clotting Time of a Mixture of Oxalated and Prothrombin-Deficient Plasma.*

Initial Concentration of Thrombin	Clotting Time*	
	Patient's Plasma	Control Plasma
units/cc.	*sec.*	*sec.*
10.0	26	14
5.0	94	29
2.5	∞	70

*Clotting time at 37°C. of a mixture of 0.1 cc. of oxalated plasma, 0.1 cc. of barium-sulfate-absorbed normal plasma and 0.1 cc. of a solution of bovine thrombin, serially diluted with buffer.

solution was tested at 37°C. in Pyrex tubes with an internal diameter of 8 mm. The clotting time of this mixture was 27.3 seconds with the patient's and 23.2 seconds with normal plasma. However,

TABLE 2. *Effect of Thrombin on the Clotting Time of a Mixture of Oxalated Plasma and Fibrinogen.*

Initial Concentration of Thrombin	Clotting Time*		
	Patient's Plasma	Control Plasma	Barbital Buffer†
units/cc.	*sec.*	*sec.*	*sec.*
10	17	12	10
5	26	20	16
2.5	71‡	40	26
1.25	∞	57	38

*Clotting time at 37°C. of a mixture of 0.1 cc. of oxalated plasma, 0.1 cc. of a solution of bovine fibrinogen (maximal concentration 250 mg. per 100 cc.) and 0.1 cc. of a solution of bovine thrombin, serially diluted with buffer.

†Substituted for oxalated plasma.

‡Poor clot.

it is possible that the thrombin inhibitor interfered with the accuracy of this test.

As has been described, the clot that formed when thrombin was added to whole blood lysed after

TABLE 3. *Fibrinolytic Activity of Oxalated Plasma.**

Source of Plasma	Initial Concentration of Plasma							
	1:10	1:20	1:40	1:80	1:160	1:360	1:640	0
Patient ...	+	+	+	±	0	0	0	0
Control ..	0	0	0	0	0	0	0	0

*Fibrinolysis (+) observed in a mixture of 0.3 cc. of oxalated plasma, serially diluted with buffer, 0.3 cc. of bovine fibrinogen solution (maximal concentration, 250 mg. per 100 cc.), and 0.1 cc. of a bovine thrombin solution containing 10 units per cc. The mixture was incubated at 37°C. for 24 hours.

it was incubated at 37°C. for forty minutes. When thrombin was added to freshly drawn blood, clots appeared promptly. The clots were kept at room temperature for twenty minutes, and then incubated at 37°C. in a water bath. These clots

*Obtained through the courtesy of the Chilcott Company, Morris Plains, New Jersey.

lysed fifty-six minutes after the blood was drawn. It thus appeared that excessive plasma proteolytic activity may have contributed to the patient's hemorrhagic state. The proteolytic activity of the plasma was tested by measurement of its ability to lyse bovine fibrin clots. The patient's plasma, diluted almost two hundred times, digested the clots in twenty-four hours. In contrast, normal plasma will not digest such clots in this period (Table 3). Human plasma has the ability to inhibit the proteolytic activity of plasma. The inhibitory activity of

TABLE 4. *Protease Inhibitory Activity of Oxalated Plasma.*

Initial Concentration of Plasma	Concentration of Plasma Proteolytic Enzyme	Clot Lysis Time*		
		Patient's Plasma	Control	Buffer†
	units/cc.	*min.*	*min.*	*min.*
1/80	2.5	33	24	—
1/160	2.5	18	18	—
1/320	2.5	18	18	—
1/640	2.5	17	17	—
0	2.5	—	—	14
0	1.25	—	—	30
0	0	—	—	∞

*Clot lysis time at 37°C. of a mixture of 0.3 cc. of bovine plasma proteolytic enzyme, 0.3 cc. of oxalated plasma, serially diluted with buffer, 0.1 cc. of bovine thrombin solution (10 units per cc.) and 0.3 cc. of bovine fibrinogen solution (maximal concentration, 250 mg. per 100 cc.). The enzyme and plasma were incubated at 37°C. for 10 minutes before the addition of thrombin and fibrinogen.

†Substituted for oxalated plasma.

the patient's plasma against bovine plasma proteolytic enzyme was not unusual (Table 4).

Slight thrombocytopenia was present, the platelet count being 144,000.

Discussion

Weiner, Reid and Roby[7] have demonstrated that amniotic fluid is thromboplastic, initiating the conversion of prothrombin to thrombin in the presence of calcium. In animal experiments the slow intravenous administration of small amounts of thromboplastin may result in intravascular defibrination.[8] For this reason, Weiner and Reid[2] suggested that the hemorrhagic phenomena in patients with amniotic-fluid embolism were the results of intravascular clotting. They postulated that this clotting defibrinated the maternal blood, which was then unable to clot in a normal manner.

As Weiner and Reid predicted, the concentration of fibrinogen was greatly diminished in the plasma of the patient described above. Several other clotting defects were present. The patient's oxalated plasma inhibited the clotting action of thrombin, and there was slight thrombocytopenia. It is of interest that thrombocytopenia and excessive thrombin-inhibitory activity were associated with afibrinogenemia in a patient with septic abortion, acute yellow atrophy of the liver and bacteremia due to *Escherichia coli*.[9] Furthermore, these defects

could be reproduced in dogs by the intravenous injection of sufficient homologous thromboplastin to cause partial or complete defibrination.[10, 11]

The patient's plasma was excessively fibrinolytic. It is not clear to what extent this fibrinolytic activity contributed to her hemorrhagic state. In rare cases bleeding phenomena have been associated with increased plasma proteolytic activity. In such patients, shed blood may be incoagulable. In 1 case, adequate amounts of fibrinogen were present in the circulating blood, but the fibrinogen seemed to be destroyed before clotting could take place.[6] In the case reported above, sufficient fibrinogen remained in the blood fifty-five minutes after it was drawn to form a firm clot when thrombin was added. Nevertheless, excessive fibrinolytic activity was demonstrable in vitro in several ways. The pathogenesis of excessive plasma fibrinolytic activity is still unexplained. Tissue particles are said to activate the proteolytic enzyme of plasma.[12] However, Weiner, Reid and Roby[7] were of the opinion that amniotic fluid did not initiate fibrinolysis. The manner in which hemorrhagic states develop in association with excessive plasma proteolytic activity requires further study.

Summary

A patient who died eleven and a half hours post partum after a prolonged period of shock is described. At autopsy, there was evidence of embolization by amniotic fluid. Three and a half hours after the appearance of the symptoms of shock, there were signs of a generalized hemorrhagic state. The patient's blood appeared to be incoagulable. This clotting defect was associated with hypofibrinogenemia, excessive plasma thrombin-inhibitory activity, slight thrombocytopenia and increased plasma fibrinolytic activity.

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TORSION OF THE SPERMATIC CORD*

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BOSTON

TORSION of the spermatic cord resulted in loss of the involved testis in approximately 75 per cent of cases reviewed in the literature by Riba and Schmidlapp.[1] Indifference on the part of the physician causes such a loss. With early diagnosis and surgical correction, potentially all involved testes could be saved. These facts have prompted us to review the cases treated at the Veterans Administration Hospital, West Roxbury, Massachusetts.

The condition is uncommon, occurring in 9 of 40,000 patients admitted to this hospital from 1946 through 1952. The average age of the patients was twenty-two years.

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Etiology and Pathology

Embryologically, the testis follows the processus vaginalis, an outpouching of the embryonal peritoneum, into the scrotum from the posterior abdominal wall. The testis becomes partially invested with the processus vaginalis. As embryologic development continues, the processus vaginalis becomes separated from the peritoneum, forming the vaginal sac.

Normally, the testis and epididymis are fixed within the vaginal sac. There are strong attachments between the testis and the epididymis, which is attached to the medial wall of the scrotum. The remaining exposed portions of the testis and epididymis are covered with visceral tunica vaginalis, which in turn is reflected upon the scrotal wall as the parietal tunica vaginalis forming the vaginal sac. None — or a very small portion — of the lower spermatic cord is covered with tunica vaginalis;

These anatomic arrangements (Fig. 1) afford firm fixation of the testis and epididymis.

The basic deformity that permits torsion of the spermatic cord is an extension of the tunica vaginalis to invest the entire testis, epididymis and lower cord. The visceral tunica vaginalis reflects from the spermatic cord to form the parietal tunica vaginalis. Thus, the testis and epididymis are suspended free in the vaginal sac, making torsion possible (Fig. 1).

The force motivating and maintaining torsion is unknown. Trauma was formerly thought to play a role, but many cases are reported to have occurred during sleep. Movements of the lower extremity at this time are thought to be a contributing factor.

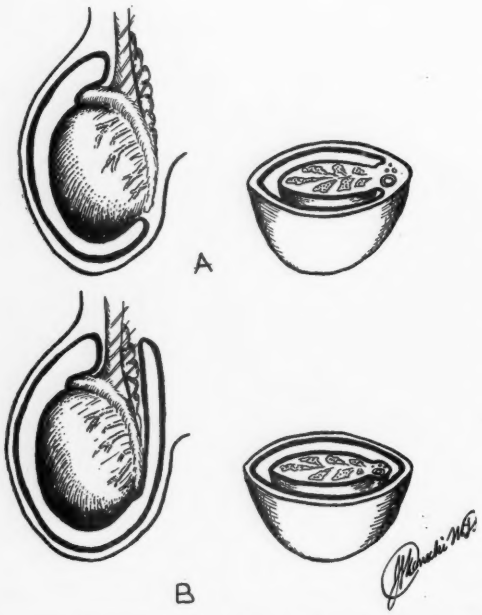

FIGURE 1. *Anatomic Intrascrotal Relations, Showing the Normal Appearance* (A) *and the Abnormal Situation in Torsion of the Spermatic Cord* (B).

Muschat,[2] after studying serial sections and reconstructions of the spermatic cord, demonstrated that in torsion the cremaster-muscle fibers were in a rotary manner and, instead of being in an external position in the cord, took a central location. He believed that this abnormal arrangement of the cremaster muscle occurs with torsion, spasm of the muscle being the motivating force.

Some authors state that the left testis turns in a clockwise and the right in a counterclockwise direction.[3] This finding was substantiated in 5 cases of this series personally observed by us. The torsion may be through a half turn or four or five complete turns; nevertheless, sufficient circulatory embarrassment usually occurs to cause infarct necrosis within eight to twelve hours of the onset in untreated cases.

Diagnosis

The most striking symptom of this condition is the sudden onset of severe, unrelenting testicular pain. The pain is usually well localized, but may radiate to the groin or flank. Unlike the pain in inflammatory conditions of the intrascrotal contents, it is not relieved by elevation of the scrotum (Prehn's sign).

The pain is so severe that medical attention is sought immediately. In our experience, this was an important consistent finding. There may be nausea and vomiting. The temperature is slightly elevated or normal. There is marked prostration, seemingly out of proportion to the pathologic process.

The course of this disease is divided into an early and late stage upon which we base our differential diagnosis and treatment. If the testis is to be saved, diagnosis and treatment must be made in the early stage, before the later changes are apparent.

In the early cases, the local changes are few. The involved testis is high in the scrotum and is exquisitely tender, making palpation impossible. Ewart and Hoffman[3] mention abnormal position of the epididymis, which is normally posteromedian to the testis, this relation changing according to the degree of torsion observed.

During the first few hours after onset, laboratory findings are normal, as in Case 1.

A past history of one or more episodes of testicular pain is frequently given. In the intermittent type of torsion, the pain is severe, lasting five to thirty minutes, and is accompanied by tenderness. It subsides rapidly without treatment. This is due to recurrent torsion, which resolves itself spontaneously. In some cases, when the torsion is frequent and severe enough, the patient seeks medical advice during the interval between attacks, as in Case 2.

The changes observed in the late stage are due to infarct necrosis of the testis and epididymis. The skin of the scrotum becomes edematous and reddened. The scrotal contents are markedly enlarged, confluent and adherent to the scrotal wall. The pain subsides gradually over a period of several days, and mild tenderness remains, being much less noticeable than in the usual case of acute epididymitis. Many of our patients were in this stage when first seen. The diagnosis was made from the history, since the physical findings were indistinguishable from those in other inflammatory conditions. If epididymoorchiectomy is not done, atrophy will occur.

The problem of differential diagnosis varies with the stage of the disease. In early cases, before local changes besides tenderness follow the sudden onset

of extreme pain, torsion of the hydatid of Morgagni and trauma must be considered; with the former, the tenderness is localized at the upper pole of the testis, and with the latter, there is a history of injury. As tumefaction, redness and edema ensue, acute epididymitis, tumor, strangulated inguinal hernia, chronic epididymitis, spermatocele, hydrocele and orchitis must be considered. The history of sudden onset of pain is the main differential point. If these conditions are found upon exploration of the scrotum for suspected torsion, little is lost, since most of them are surgical emergencies.

Treatment

This condition constitutes a true surgical emergency. Early diagnosis and prompt surgical treatment are mandatory. All too often, patients are merely given morphine and observed during the critical hours when the testis could be saved.

The involved testis is exposed through the anterolateral scrotal wall. The torsion is reduced. The parietal tunica vaginalis is excised, and the testis is fixed to the medial scrotal wall with two or three widely placed sutures. Adhesions readily form between the testis and the scrotal wall, giving firm fixation. When the recurrent type of torsion is suspected in a patient complaining of several episodes of testicular pain, exploration of the scrotum is indicated. If orchiopexy is not done, testicular gangrene may occur in the future, or there may be progressive damage to the testis by repeated vascular insults.

Because of the high incidence of bilateral torsion (Ewart and Hoffman[3] found 26 out of 489 cases in the literature), the same procedure is carried out on the opposite side.

The possibility of interference with spermatogenesis when this method is used has been considered. A follow-up study in 4 cases with this problem in mind was carried out, and no such interference could be demonstrated.

If the testis is not viable, orchiectomy is done. Orchiopexy is carried out on the opposite side.

When the patient is in a condition or place not conducive to surgery, reduction of the torsion may be attempted manually through the scrotum. If this is successful, surgical correction should be done at the first suitable time and not postponed indefinitely, as it often is.

Case Reports

Case 1. J. A. W. (R39446), a 25-year-old clerk, was admitted to the hospital on January 13, 1952, with severe and unrelenting pain in the right testicle of sudden onset. The family physician was consulted shortly after onset, and codeine was prescribed. This failed to relieve the pain, and the patient was referred for admission 4½ hours after onset.

The past history revealed several previous attacks of testicular pain.

Physical examination showed the patient to be in acute distress with a normal temperature and a pulse of 90. The right testis was at the level of the external inguinal ring and too tender for palpation. There were no visible changes in the adjacent scrotum. Laboratory data were normal.

Forty-five minutes after admission, exploration revealed that the right spermatic cord was twisted through approximately 720° in a counterclockwise direction. The testis and adnexa were markedly cyanotic, but after untwisting, circulation was promptly re-established. The typical high investment of the tunica vaginalis with inadequate fixation of the testis was present. Bilateral orchiopexies were done.

Recovery was uneventful. Examination 2 months after operation revealed normal scrotal contents with no atrophy. The ejaculate volume was 4 cc., with a pH of 8.5 and normal viscosity. The sperm count was 93,000,000, and motility and morphology were normal.

This patient presented the classic symptoms, physical findings and pathology of early torsion of the spermatic cord. The case illustrates that potentially all testes can be saved in this condition with prompt diagnosis and treatment.

Case 2. R. L. (R40017), a 24-year-old cab driver, was referred to the hospital on February 6, 1952, because of recurrent attacks of pain in the left testicle of 10 years' dura-

Figure 2. *Investment of the Lower Spermatic Cord, Epididymis and Testis with the Tunica Vaginalis. An artificial torsion has been made.*

tion. The pain was unprovoked and sudden in onset, lasting as long as 12 hours and subsiding spontaneously without therapy. Each time the testis became swollen and tender. The attacks were increasing in severity and frequency, occurring at approximately weekly intervals, when the patient was admitted. He was childless, after 4 years of married life.

Physical examination was negative. A diagnosis of recurrent torsion of the left spermatic cord was made, and surgical exploration was advised.

At operation, the left vaginal sac was found to extend to the level of the internal inguinal ring, without communication with the peritoneal cavity. The testis and appendages were suspended free in the sac, being completely invested by tunica vaginalis (Fig. 2). A similar deformity was observed on the opposite side, except for adhesions between the epididymis and scrotal wall, which caused fixation and explained the absence of symptoms. Orchiopexies were carried out in the manner described.

On follow-up examination 3 months later, the patient had been completely relieved of pain. The scrotal contents were normal. There was no loss of libido. Examination of the ejaculate revealed a volume of 4.5 cc., normal viscosity and normal pH. The sperm count was 15,000,000, with 65 per cent motility and normal morphology.

This case was typical of the recurrent type of spermatic-cord torsion. The symptomatology was completely relieved by correction of the abnormality. The patient was childless preoperatively, and semen examination postoperatively revealed relative infertility. Testicular malfunction incident to recurrent torsion may have contributed to this problem.

Case 3. R. K. T. (R36967), a 24-year-old student, was admitted to the hospital on September 3, 1951, with pain and swelling of the right scrotum. While working as a bellhop 3 weeks prior to admission, he had suddenly experienced a severe, unrelenting pain in the right testicle. A physician was consulted immediately, who advised a suspensory. During the ensuing 2 weeks the patient was treated with various antibiotics and local applications by 5 different physicians.

Physical examination was negative except for the right scrotum, which was reddened and edematous. The testis and epididymis were a confluent mass measuring 9 by 4 cm. and adherent to the scrotal wall. There was moderate tenderness. The prostate was normal. A diagnosis of acute epididymitis was made, and the patient was treated accordingly. Lack of response to treatment prompted reconsideration of the history. Torsion was then suspected, and operation advised.

Upon exploration, the typical high investment of the tunica vaginalis was found. The right spermatic cord was twisted through 540° in a counterclockwise direction. The testis and epididymis were gangrenous and were removed. Eight months after discharge, the left testis was normal. There was no loss of libido, but the patient refused to submit to semen examination.

Case 4. J. F. M. (R8649), a 28-year-old veteran, was admitted to the hospital on June 26, 1946. Three days before admission, while he was riding in an automobile, pain in the right testicle had suddenly occurred. Twenty-four hours later, his family physician was consulted, and admission was arranged.

Upon admission, 72 hours after the onset of pain, physical examination was negative except for a slightly tender mass in the right scrotum, with edema and redness of the adjacent scrotum. A testicular tumor was suspected.

Exploration revealed a gangrenous testicle and epididymis due to torsion with the typical deformities. Orchiectomy was done. Recovery was uneventful; follow-up information was not obtainable.

Case 5. A. O. (R25562), a 22-year-old man, was admitted to the hospital on August 25, 1949. Five weeks before admission, he had been awakened from sleep by severe pain in the left testicle. On the following morning, the left testis was lemon sized, and the family physician advised bed rest and local applications. Subsequently, the pain subsided gradually, but the swelling persisted.

Physical examination was negative except for an enlarged, confluent, nontender intrascrotal mass.

A testicular tumor was suspected, but exploration revealed spermatic-cord torsion, with the typical findings. Orchiectomy was necessary, and orchiopexy was done on the opposite side. Recovery was uneventful, but follow-up information is unavailable.

Case 6. J. N. R. (R26152), a 25-year-old veteran, was admitted to the hospital on October 4, 1949. Six days prior to admission, he had been awakened by severe pain in the left testicle. A few hours later, swelling was noted. The family physician was consulted; penicillin and codeine were prescribed. The pain and swelling persisted and were accompanied by nausea and vomiting.

On admission physical examination was negative except for a large, tender mass in the left scrotum, with edematous adjacent skin. Torsion of the spermatic cord was suspected.

Exploration revealed the left spermatic cord to be twisted through 180°, in a clockwise direction. Orchiectomy was necessary, as well as contralateral orchiopexy. Two and a half years postoperatively, the remaining testis appeared normal. There was no loss of libido, and the patient's wife was pregnant at the time of examination.

Case 7. P. P. A. (R26596), a 26-year-old cab driver, was admitted to the hospital on November 2, 1949. One hour after being awakened by a sudden severe pain in the left testicle the patient had been admitted to the accident room of a general hospital. After 14 hours of sedation and observation, he was transferred to the West Roxbury Veterans Hospital.

The past history revealed a similar attack of testicular pain, which had subsided spontaneously.

Physical examination showed the left testis to be retracted to the level of the external ring. The overlying scrotal skin was reddened and edematous. The testicle was indurated and tender. The white-cell count was 12,400, with 72 neutrophils.

Exploration revealed a gangrenous testis and epididymis, with the typical deformities of torsion. Orchiectomy and contralateral orchiopexy were performed. There was no loss of libido, and the patient's wife had a child after the operation.

Case 8. F. E. H. (R37657), a 27-year-old man, was admitted to the hospital on October 8, 1951. Eleven days before admission, severe pain in the left testicle had suddenly occurred. The family physician was consulted immediately, and morphine was administered. During the following 4 days the pain gradually subsided, but slight tenderness and swelling persisted. After local applications and penicillin failed to provide relief, the patient was referred for admission.

Physical examination revealed a confluent, tender mass in the left scrotum, with overlying edematous skin. A diagnosis of infarct necrosis of the testis secondary to torsion of the spermatic cord was suspected.

Exploration showed a gangrenous testicle and adnexa, with the typical deformities of torsion. Orchiectomy and contralateral orchiopexy were carried out. Recovery was uneventful. Follow-up examination 6 months postoperatively revealed a normal right testis. Libido was normal. The patient refused to submit to semen examination.

Case 9. H. M. (R35285), a 35-year-old mechanic, was admitted to the hospital on May 17, 1951. Four days prior to admission, severe pain in the right testicle suddenly occurred. The family physician, who was consulted immediately, prescribed bed rest, local applications and penicillin.

Physical examination revealed a reddened, edematous scrotum with an underlying tender mass. The patient was treated for acute epididymitis but with no response to treatment, exploration was advised.

Operation showed torsion, with a gangrenous testicle and epididymis. Orchiectomy was performed. Recovery was uneventful; no follow-up was obtainable.

The last 7 cases are typical of the course and outcome in spermatic-cord torsion. Temporizing on the part of the patient or physician resulted in gangrene, with loss of the testis. After gangrene had been established, the differential diagnosis was more difficult, the condition being most frequently confused with acute epididymitis and testicular

tumor. Contralateral orchiopexy was done in most cases, and follow-up study of a few patients revealed no impairment of testicular function.

Summary

The clinical characteristics, pathology and treatment of spermatic-cord torsion are reviewed. Seven cases resulting in orchiectomy and 2 cases in which the testis was saved are presented. The necessity for early diagnosis and treatment is emphasized.

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MEDICAL PROGRESS

PEDIATRICS (Concluded)*

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BOSTON

Congenital Malformation of the Heart

The pioneer advances in cardiac surgery of Gross[75] and Blalock[76] have greatly stimulated interest in the problems of congenital malformations of the heart. Surgical procedures that have been devised include treatment of patent ductus arteriosus, congenital vascular ring, coarctation of the aorta, tetralogy of Fallot, pulmonary stenosis, mitral stenosis and other anomalies of blood vessels.

Cardiac catheterization is a safe and useful procedure in the study of cardiopulmonary physiology as well as in the diagnosis of congenital malformations of the heart. The work of Cournand,[77, 78] Bing,[79-82] Dexter,[83] McMichael[84] and others on catheterization of the chambers of the heart and great blood vessels has been a major factor in furthering understanding of the changes in the hemodynamics of the circulation produced by the various congenital cardiac anomalies.

The catheter used is a thin-walled, radiopaque instrument, inserted into the median basilic vein under local novocain anesthesia. A glucose-water solution containing heparin is allowed to run through the catheter during the procedure. Under fluoroscopic control the catheter is passed into the superior vena cava, the right auricle and the right ventricle and out the pulmonary artery. Samples of blood are withdrawn from the pulmonary artery, the right ventricle and the right auricle and both venae cavae. The oxygen content is determined on all samples, including one from the femoral artery. Spot films are taken at the time a sample of blood is withdrawn to note the exact location. The normal oxygen variation between the superior vena cava and the right auricle is 1.9 vol. per cent; between the right auricle and the right ventricle, 0.9 vol. per cent; and between the right ventricle and the pulmonary artery, 0.5 vol. per cent. Pressure studies are also recorded in the various sites.

Cardiac catheterization may aid in the diagnosis of congenital malformations of the heart by providing information about the presence of intracardiac or great-vessel shunts, partial obstruction to outflow of chambers and, in some cases, anomalous origin or course of vessels.

Cardiac catheterization is of value in establishing the presence of pulmonary stenosis, in recognition of defects of the auricular and ventricular septums when the clinical diagnosis is in doubt, in investigation for patent ductus arteriosus when a typical continuous machinery murmur is absent, and in the diagnosis of pulmonary hypertension. Cardiac catheterization is of particular value in the study of left-to-right shunts.

In 1937 Castellanos, Pereiras and Garcia[85] reported the successful radiographic demonstration of the cardiac chambers and great blood vessels in infants and children through the use of a radiopaque medium by a technic they named "angiocardiography," a safe and practical diagnostic procedure in the adult and child. Recent technical achievements in angiocardiography permit precision in the definition of malformations of the heart.[86-89]

Angiocardiography gives an objective visual demonstration of the cardiac chambers and of the great vessels. As aptly stated by Gasul and Warnick,[90] it gives the clinician the only means of "dissecting" the great vessels and the chambers of the heart during life, as seen in serial angiocardiograms taken at specific intervals.

The procedure yields valuable information in the study of the following conditions: dextroposition of the aorta; the size and position of the pulmonary arteries; pulmonary stenosis, especially in

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the right oblique view; complete transposition of the great vessels; coarctation of the aorta; persistent left superior vena cava; and dextrocardia. In a few cases it may help to confirm the diagnosis of patent ductus arteriosus by the indirect sign of the reopacification of the pulmonary artery or by demonstration of a localized dilatation of the aortic arch in the region of the insertion of the ductus. It is of value in demonstrating right-to-left shunts.

Angiocardiography should be reserved for the rare problem cases, however, since cardiac fluoroscopy is still recognized as the most useful conventional method in the diagnosis of congenital malformations of the heart. Information derived from cardiac fluoroscopy in conjunction with electrocardiographic and clinical studies will suffice for a reasonably accurate diagnosis in the majority of cases.

The scope of surgery in patent ductus arteriosus has broadened since Gross[91] first described the technic for ligation of this persistent fetal shunt between the aorta and pulmonary artery. In the young adolescent or child whose physical growth has been retarded by patent ductus arteriosus, obliteration of the shunt by ligation or division of the ductus has a definite effect in increasing the peripheral blood flow and stimulation of subsequent growth and gain in weight. In cardiac embarrassment or failure, elimination of the ductus greatly reduces the work of the heart and improves cardiac reserve. In the presence of subacute bacterial endocarditis, surgical closure of the ductus is usually followed by improvement or cure; the infection is an indication for, not a contraindication to, surgery.

Gross and Neuhauser[92, 93] have described five types of anomalies of the great vessels of the superior mediastinum that can compress the esophagus or trachea. These anomalies must be considered in any infant with persistent feeding or respiratory difficulty. Compression of the esophagus, and especially of the trachea, by the posterior and anterior arches of the ascending aorta usually causes difficulty in swallowing, with stridor or "crowing," and is conducive to respiratory infections. The infant holds his head in hyperextension, which allows more room for the trachea; it will be observed that the infant may quickly show signs of difficulty on flexion of the head. A tracheogram with Lipiodol aids in the diagnosis. Posterior esophageal compression and an anterior tracheal mass are indicative of an encircling ring. A right aortic arch in itself causes little difficulty. The location of the ligamentum arteriosum determines if there is compression of the trachea.

When the ligamentum arteriosum lies anterior and to the right of the trachea, it does not cause any difficulties; however, if it passes to the left of the trachea and around the esophagus to reach the aorta, thus completing a constricting ring, it may produce symptoms that are similar to those of double aortic arch but are not usually so severe. Surgical relief includes division of the ligamentum arteriosum, and the left subclavian artery must be severed if it passes behind the esophagus.

An anomalous innominate artery arising further along on the arch than usual may cause compression of the trachea. A tracheogram will aid in the diagnosis by revealing a filling defect. In this anomaly, respiratory distress is more outstanding than the feeding difficulty. Surgical relief involves attaching the anomalous vessel to the sternum.

An aberrant subclavian artery may compress the esophagus and cause difficulty in swallowing. On barium swallow, with the patient in the oblique position, a filling defect is easily demonstrated.

In most patients with coarctation of the aorta, serious or even fatal complications may develop in midlife owing to hypertension, rupture of the aorta or bacterial infection at the site of the narrowing. Independently of each other, Gross[94] and Crafoord[95] were the first to devise a procedure whereby the segment of narrowing was resected and the two ends of the aorta brought together in an end-to-end anastomosis. The technic is most easily applied to the postductal type of coarctation, usually referred to as the "adult type." In this type, surgical removal of the coarcted segment is best carried out in childhood because sclerosis of the aorta makes suturing technically difficult and increases the operative risk. The preductal form, or "infantile type," is often so extensive that there is an insufficient blood supply to the left subclavian artery; resection may be difficult or impossible. The possibility of surgical relief in coarctation of the aorta makes early diagnosis most important. Palpation of the femoral pulses and blood-pressure determination should be done as part of every physical examination in infancy and childhood.

The defect of greatest physiologic significance in patients with the tetralogy of Fallot is the pulmonary stenosis, which decreases the blood flow to the lungs. To increase the net amount of oxygen supplied to the tissues, Blalock[96] devised an operation that involved anastomosis of a systemic artery — usually the subclavian — to the pulmonary artery, allowing the mixed systemic blood to pass through the lungs and become fully oxygenated. Potts[97] next accomplished the same result by anastomosis of the aorta to the pulmonary artery. Both procedures have been widely accepted. Brock[98] considered that direct relief of the pulmonary stenosis would be a more desirable end and introduced an operation to accomplish this. It has attained less popularity than the shunting procedure, the main objection to the direct attack on the pulmonary stenosis being that in the tetralogy the obstruction is usually in the form of a partial membrane across the outflow tract of the right ventricle and its removal is too dangerous. Bailey and his associates[99] regard the objection as not entirely valid and believe

that Brock's is the operation of choice, pointing out its physiologic superiority to the Blalock and Potts procedures. In their small series, over half the patients either had true valvular stenosis or could be treated as such, and the operative mortality was no greater in those undergoing infundibular resection than in those with valvotomy. It certainly seems that from the physiologic point of view the direct procedure is the operation of choice. No true comparison can be made between patients treated with shunting procedures and those treated with the Brock type of operation. A long-term follow-up study will be necessary before a definite evaluation can be made of their relative over-all merits.

Pulmonary stenosis may exist without a defect of the ventricular septum and may be "pure" — that is, with no avenue of intracardiac shunt — or with an atrial septal communication such as a patent foramen ovale. Certain important differences in clinical manifestations are found. If there is no auricular communication, there is no cyanosis, and the patient will show no symptoms until there is a degree of heart failure; shortness of breath and easy fatigue will then appear. There is no argument about the operative procedure in these cases: valvulotomy is indicated. The choice of patients for the operation is at present a matter of some contention. One group believes that a patient who is without symptoms should not be operated on. Others are of the opinion that even without symptoms, operation should be performed in a patient who has a high pressure in the right ventricle as determined by cardiac catheterization. The operative mortality is low in this malformation, and the latter view appears the more logical.

Defects of the auricular septum have been of great interest to surgeons for the past several years. Of a number of ingenious procedures used to close defects in laboratory animals, a few have been adopted as applicable for use in human patients. Bailey and his co-workers[100] recently reported a promising method of closure that involves suturing the wall of the dilated right atrium to the margin of the defect and thus completely interrupting the shunt. If such procedures prove applicable for general use, many patients will be greatly benefited, for this lesion is frequently the cause of invalidism. More recently, Gross[101] has effected closure by suturing an onlay sheet of plastic material over the opening.

Treatment of Bacterial Meningitis

There are today at least six effective agents for treatment of meningitis due to *Haemophilus influenzae*: the sulfonamides, specific rabbit antiserum, streptomycin, aureomycin, chloramphenicol and terramycin.[102-106] The results reported from various clinics indicate that the optimal treatment at present is streptomycin intramuscularly for twenty-four hours, or for forty-eight hours combined with sulfadiazine or Gantrisin and one of the wide-spectrum antibiotics such as aureomycin, terramycin or chloramphenicol. During the first twenty-four or forty-eight hours, medication is best given parenterally rather than orally. Although the mortality has decreased with this treatment, the incidence of cerebral damage among the survivors has increased, suggesting that the greater number of survivors may be accounted for by survival of a larger number of damaged children. Reports indicate that streptomycin given for even a few days may be productive of disturbed vestibular function. Intrathecal administration of streptomycin is still being used during the first twenty-four hours of treatment in some clinics but in a smaller dosage than previously recommended.

McKay et al.[107] and Smith and his associates[108] have reported the occurrence of subdural collections of fluid in patients with influenzal meningitis. This complication has variously been reported as occurring in as many as 50 per cent of patients recovering from meningeal infection caused by pyogenic agents. The fluid is similar to that found in subdural hematomas of traumatic origin. McKay and his co-workers recommend the following indications for subdural taps in patients with meningitis: fever after forty-eight to seventy-two hours of treatment; positive cerebrospinal-fluid cultures after forty-eight hours of treatment; convulsions after apparent subsidence of infection; focal convulsions at any time; vomiting after apparent subsidence of infection; any gross neurologic abnormality during the immediate convalescent period; and an unsatisfactory course on the basis of clinical judgment. Subdural collections of fluid are found less frequently in older children with closed fontanels.

The optimal treatment of meningococcal meningitis is sulfadiazine or Gantrisin given parenterally during the first twenty-four hours and thereafter by mouth as tolerated; penicillin is also effective. Fulminating bacteremia associated with signs of Waterhouse–Friderichsen syndrome has been successfully treated with cortisone and specific therapy. Hodes et al.[109] report success with the following dosage schedule: 50 mg. intravenously, 50 mg. intramuscularly and 50 mg. orally on admission; 50 mg. orally or intramuscularly after twelve hours and 25 mg. orally twice daily for five or six days. The eosinophilic response can be used as an early index of the adequacy of adrenocortical response to the stress of infection.

Penicillin in large doses combined with sulfadiazine is still the treatment of choice of pneumococcal and streptococcal meningitis.[110] One intrathecal dose of penicillin of 5000 to 10,000 units is recommended in pneumococcal meningitis. Penicillin is the most effective single agent in the treatment of streptococcal meningitis, usually being given intrathecally every day for the first four days of therapy. Aureomycin in combination with peni-

cillin is also effective. The combined use of streptomycin and sulfadiazine has been successful in the treatment of meningitis caused by *Escherichia coli*.

A great deal of investigative work is still being conducted on the treatment of tuberculous meningitis. Streptomycin in combination with para-aminosalicylic acid or Promizole has been employed with varying success. Smith and her associates[111, 112] recently reported the use of an intrathecal purified protein derivative of the tubercle bacillus in addition to the usual treatment with streptomycin. The results suggest that PPD may aid in the removal of fibrinous exudate. At present the therapy is being employed in patients with tuberculous meningitis whose prognosis is poor and in those with depression of the sensorium or with other signs of cerebral damage.

Leukemia

Farber and his colleagues,[113] in June, 1948, were the first to report favorable experience with the use of folic acid antagonists, aminopterin and related compounds, in the treatment of children with leukemia.[114] Subsequent reports[115-121] from others bear out the finding that aminopterin and other folic acid antagonists (a-methopterin and amino-an-fol) produce amelioration of symptoms, with remissions of the leukemic process and lengthening of the lives of these patients.

Of the several compounds used, aminopterin is the most effective in its action on the leukemic process, and yet one of the most toxic. After four to seven days the following effects on the leukemic process are noted[122-128]: white-cell counts tend to return to normal levels, whether initially depressed or elevated, and the percentage of polymorphonuclear neutrophils increases to normal levels; lymph nodes and spleen decrease in size; blast cells disappear from the peripheral blood; reticulocyte counts and the hemoglobin increase, and the platelet count improves toward normal; and leukemic cells tend to decrease or disappear from the bone marrow, and a hypoplastic or normal marrow may be found. Hematologic remissions are accompanied by clinical improvement, as manifested by increased appetite and disappearance of fever, bone pain and purpuric lesions. Remission may occur within one or two weeks of treatment, varying in duration from a few weeks to eighteen months. The remission rate in children treated for acute lymphatic leukemia averages about 50 per cent in various reported series.

Toxic effects such as stomatitis and ulceration of the mouth and gastrointestinal tract are frequent. The symptoms of toxicity in patients under treatment are loss of weight, anorexia, stomatitis, alopecia, erythema or purpuric skin rash, abdominal distention and pain, diarrhea with blood and mucus, melena and pancytopenia and aplasia of the bone marrow. Individual tolerance to the drugs varies greatly, some patients tolerating therapeutic doses daily for weeks or months whereas in others the drug must be discontinued after a few days' trial because of a bleeding tendency. Most children have tolerated doses of 0.5 to 1.0 mg. of aminopterin daily. These drugs must be given under carefully controlled conditions with daily blood counts and frequent bone-marrow examinations during the early stages of therapy. When the individual tolerance or maintenance dose of the patient has been determined, blood counts at weekly intervals may suffice. It must be emphasized that the folic acid antagonists are toxic drugs, to be used with extreme care, and that they prolong life but do not cure the leukemic process.[129-135]

ACTH and Cortisone

Sufficient time has elapsed to permit clinical evaluation of ACTH and cortisone in a wide variety of conditions in infants and children. The ready availability of these compounds makes it advisable to give careful consideration to the indications for their use. These powerful physiologic agents have not proved as valuable as anticipated. The physiologic and chemical changes accompanying therapy with them are becoming increasingly apparent, but the basic mechanism of action remains to be clarified. As pointed out by Hench et al.,[136, 137] ACTH and cortisone are still experimental tools, to be used judiciously pending further information on the fundamental processes. Since these substances are used chiefly for their pharmacodynamic action, side effects must be guarded against. The drugs do not "cure" any disease; they seem to produce symptomatic relief in many cases, but they do not permanently alter the basic disease. Table 1 lists the indications for their use.

Table 1. *Indications for ACTH or Cortisone Therapy.**

Clear-cut Indication	Indication in Selected Cases of Acute Disease	Of Possible Value in Management
Inflammatory disease of eye	Rheumatic fever	Rheumatoid arthritis
Status asthmaticus	Acquired hemolytic anemia	Nephrotic syndrome‡
Addison's disease†	Severe hypersensitivity reactions	Ulcerative colitis
Adrenocortical hyperplasia‡	Idiopathic hypoglycemia	Regional enteritis
Functional adrenocortical failure†		Waterhouse–Friderichsen syndrome†
		Disseminated lupus erythematosus
		Leukemia

*Adapted from the *Year Book of Pediatrics*.[138]
†Cortisone only.
‡ACTH only.

Both ACTH and cortisone generally produce symptomatic relief in allergic disorders such as bronchial asthma, hay fever,[139] angioneurotic edema, drug sensitization[140] and serum sickness. Status asthmaticus refractory to the usual therapy often responds remarkably, and the improved state lasts

from several weeks to months in many cases. After such hormonal therapy the patient frequently responds to the usual bronchodilator drugs, but this therapy should be reserved for the severe cases demanding relief that cannot be obtained by any other treatment. Cortisone has the advantage of being available as an oral preparation that yields as good results as parenteral therapy.

In selected cases of acute rheumatic fever, cortisone and ACTH given early in the course of the illness have been valuable in suppressing the acute manifestations of the disease. Within twenty-four hours many patients lose their toxic and ill appearance and feel comparatively well. Temperatures return to normal within one to five days in most cases. The appetite improves, and there is usually an actual gain in weight. Relief of painful, swollen, inflamed joints usually occurs within a week of therapy. The elevated blood sedimentation rate rapidly drops to normal concomitantly with improvement in the general condition. Many patients remain well when therapy is discontinued; others relapse, with exacerbation of symptoms and signs. The blood sedimentation rate may again rise during such a relapse. It is too early to determine whether ACTH and cortisone will prevent serious cardiac damage in patients with rheumatic carditis, as suggested in earlier reports.[141-143] Long-term studies will be necessary to evaluate their ability to prevent the development of valvular lesions.

ACTH and cortisone are effective in the active stages of rheumatoid arthritis although improvement is usually not maintained, an exacerbation of symptoms and signs occurring in a high percentage of cases once the drugs are discontinued.[144-146] Permanent improvement is not to be expected in chronic cases with structural joint changes. In the acute stage of the disease stiffness of the involved joint diminishes within the first two days of treatment, with a subsequent decrease in joint tenderness, swelling and pain on motion. Accompanying these remissions there is an improvement in the general well-being of the patient. Within twelve to forty-eight hours of the discontinuance of the drugs, however, signs and symptoms begin to reappear and gradually become worse. If the hormone is readministered, a prompt remission is usually obtained.

ACTH and cortisone produce a temporary response in some cases of acute lymphatic leukemia, but relapses are common. Enlarged lymph nodes usually regress, and the blast cells disappear from the peripheral blood during a response to therapy. ACTH or cortisone has recently been used in combination with folic acid antagonists such as aminopterin in the treatment of leukemia of childhood. In some clinics, these drugs are employed when the diagnosis of acute leukemia is made, and continued until resistance to these drugs develops; treatment with the hormones is then instituted, after which a response to the folic acid antagonists may again be obtained.[147-150]

Numerous reports[151] have appeared in the literature on the effects of ACTH on children with the nephrotic syndrome. Almost all investigators agree that the hormone will induce a diuresis in about 80 per cent of these cases. Cortisone does not produce the same desired diuresis. The evidence is that ACTH does not cause a reversal of the basic mechanism producing nephrosis but is helpful only in effecting a diuresis, which usually occurs after a course of treatment, and although refractoriness does occur, another course of ACTH therapy may induce another diuresis. One child responded to six courses of therapy, but sometimes a child who responds to one or two courses may fail to respond subsequently.

Riley[152] has reported an absence of changes in the plasma sodium, bicarbonate, chloride and potassium, or in the total proteins. The total blood cholesterol usually drops considerably regardless of clinical results. Kramer et al.,[153] Lauson and his associates[154] and Rapoport and his co-workers[155] have described a decrease in proteinuria during and after ACTH therapy. Barnett has noted an increase in glomerular filtration rate occurring at the onset of diuresis in many children who had reduced rates prior to therapy. Metcoff and his colleagues[156, 157] have reported reversion to normal exchange of sodium and potassium in the renal tubule; Wedgewood and Janeway[158] have found a rise in serum complement. All the dangers associated with corticotrophin therapy—hypokaliemia, hypertension and infection — exist as potential hazards of treatment.

In the treatment of nephrotic patients, the potassium content of the diet should be increased to prevent hypokaliemia.[159] Since ACTH may mask signs of infection, prophylactic antibiotic therapy is given routinely during the course of treatment. It must be emphasized that although ACTH is a useful therapeutic agent in the management of the nephrotic patient, such treatment should be carried out only under close supervision.

Surgery

In the past both laymen and doctors believed that infants were extremely poor operative risks, and physicians advised postponement of herniorrhaphy until the child was two to five years of age. This proved a misconception, for infants tolerate anesthesia and operation as well as, or better than, older children and unquestionably better than adults. Infants rarely vomit postoperatively and retain feedings two to four hours after a general anesthetic. Atelectasis and venous thrombosis with pulmonary infarction are practically unknown postoperative complications in infants or children.

MANHATTA
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Hernia

Herniorrhaphy on infants is a safe procedure, and recurrence of the hernia is rare. Potts et al.[160] reported 1 death and 1 recurrence in 600 children. Another paper reports 506 herniorrhaphies with 1 postoperative death, which occurred in an infant with an incarcerated hernia and severe aspiration pneumonia. The hernia could not be reduced by manipulation, and the baby died eighteen hours after an emergency herniorrhaphy. Post-mortem examination revealed severe aspiration pneumonia as the cause of death. Early surgical repair relieves parents of the work entailed by the use of a truss and eliminates incarceration, which is a dangerous complication of inguinal hernia. Hospitalization for herniorrhaphy is short — usually two days. The wound is closed with subcuticular sutures so that there are no sutures through the skin to increase the likelihood of infection, and the baby can be diapered postoperatively in the usual fashion.

Imperforate Anus

In 1948 Rhoads and his associates[161] reported a one-stage abdominoperineal anoplasty for newborn infants with imperforate anus, with the rectal pouch several centimeters from the perineal skin. This is an improvement over the three-stage procedure consisting of colostomy, abdominoperineal anoplasty and closure of colostomy. The selection of newborn infants with imperforate anus for this combined one-stage abdominoperineal anoplasty is made on the basis of x-ray films of the infant in an inverted position with a lead marker on the anal dimple of the perineum. The distance from the air-filled rectal pouch to the lead marker can be measured. If the distance is 1.5 cm. or less, a perineal anoplasty is the simplest method of correcting the anomaly; a greater distance prevents an adequate operation through the perineum and is an indication for the combined abdominoperineal procedure. The one-stage operation should not be used unless the patient is in good condition. Infants who have not been given surgical attention in the first seventy-two hours of life should probably be treated by the more complicated but safer three-stage operation.

Hirschsprung's Disease

In 1948 a new concept of the pathology and treatment of Hirschsprung's disease was reported. It was observed that sigmoid colostomy completely relieved these patients of constipation and abdominal distention.[162] However, closure of the colostomy precipitated a recurrence of the disease. Reopening of the colostomy in such patients again relieved the symptoms. These facts could only be explained by the presence of a functional obstruction in the distal portion of the colon. X-ray studies of these patients revealed a curious narrowing of a portion of the distal colon, with marked dilatation of the colon above this. In some patients the narrowing was limited to the rectosigmoid and was not over 5 to 8 cm. in length. In others, the narrowing extended as far as the splenic flexure or the midpoint of the transverse colon. A technic was devised that made it possible to remove the defective colon down to the sphincter mechanism, with preservation of anal continence.

Examination of the segment of narrow bowel removed from these patients revealed an absence of ganglion cells in Auerbach's plexus. It had been known for a number of years that the distal portion of the colon in Hirschsprung's disease contained a congenital defect in Auerbach's plexus, but no clinical application had been made of this information. Physiologic studies have demonstrated that peristaltic waves of the colon do not enter the aganglionic bowel. All information indicates that Hirschsprung's disease is due to a congenital anomaly of the parasympathetic system resulting in an aganglionic segment of distal colon that has no peristalsis. This defect in function of the distal colon accounts for the severe constipation and abdominal distention seen in Hirschsprung's disease. Removal of the defective segment of bowel, with re-establishment of continuity of the colon, completely relieves the patients of their symptoms. Satisfactory results have been reported by Hiatt[163] in New York and Bodian et al.[164] in England after resection of the aganglionic bowel.

It has been noted in a group of patients with Hirschsprung's disease that some of them have an associated lesion of the urinary bladder consisting of poor or absent detrusor contractions and marked bladder enlargement. It seems plausible to explain this bladder defect as a congenital malformation of the pelvic parasympathetic system, which normally innervates the detrusor muscle. It was also found that some of these patients had increased intravesical pressure, with difficulty in bladder emptying, and these particular patients were found to have megaloureters. There was no bladder-neck or urethral obstruction. Bladder drainage of such patients demonstrated marked improvement of the upper urinary tract. The anomaly has also been encountered in patients with Hirschsprung's disease, and in such cases bladder drainage has resulted in improvement of the upper urinary tract. These patients have forceful peristalsis of the ureters and no ureterovesical obstruction, all of which indicates the lesion to be in the bladder. Careful histologic studies have revealed marked diminution in the number of ganglion cells in the bladders of patients who have the syndrome of enlargement of the upper urinary tract, with good ureteral peristalsis and with a bladder that is enlarged and has an increase in intravesical pressure with a residual urine but no mechanical obstruction. These patients were treated with bladder drainage for a period of months,

giving the upper urinary tract an opportunity to improve and the bladder a chance of becoming normal in size. After this, the patients were instructed to void at frequent intervals and to make a great effort to empty the bladder completely. Some patients have been followed for two or three years and have maintained their improvement.

Intussusception

Hydrostatic pressure for reduction of intussusception was advocated over a hundred years ago by Hirschsprung. Results were poor, and surgery gradually replaced it as a method of treatment. Recently the hydrostatic method has been revived with the use of barium enema administered during fluoroscopic observation.[165] The renewed interest has not been prompted by poor results of surgical treatment, for the mortality rate in several surgical clinics is now 2 to 4 per cent.[166] The nonsurgical treatment is advocated and is appealing because of its apparent simplicity. Although it may save the patient an operation, the treatment has serious limitations and dangers, and some believe that these shortcomings condemn the method.

Hydrostatic treatment of intussusception should not be advised by the attending physician unless the history is of less than fifteen hours' duration, the baby is in good general condition, there has been no significant amount of blood in the stool and there is no roentgenologic evidence of small-bowel obstruction. These rules are listed in an attempt to prevent intestinal perforation, which has been a complication when patients were not carefully selected for this form of treatment.

Hydrostatic reduction of intussusception should not be undertaken except in the presence of the surgeon who has the responsibility of operating on the child should the radiologist's attempts fail.

If reduction is not achieved promptly with low pressure, the procedure should be terminated and operation proceeded with. Unless this is strictly adhered to, the infant may become exhausted and a poor risk when operation becomes necessary.

A serious criticism of this method is the lack of simple, exact signs of complete reduction. Ileal components are most difficult to detect and reduce. The decision whether a Meckel diverticulum or another anomaly is the cause of the intussusception (as in about 10 per cent) cannot be made by this procedure and is a disadvantage of this form of treatment.

These limitations and dangers make it uncertain whether widespread use of hydrostatic reduction will equal the sure results and low mortality attained with surgical treatment of intussusception.

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MEDICAL INTELLIGENCE

A CONVENIENT, RELIABLE HUBLESS NEEDLE

First Lieutenant Arthur S. Rathkey, M.C., U.S.A.F.*

THE needle described below has been used successfully for over two years, with a great saving of time. I believe that it is faster in application than the plain baseless needle of Gardner[1] and less bulky than Rowbotham's[2] modification of the Gordh needle.

Figures 1 to 3 are considered sufficiently clear to allow the average hospital repairman to construct

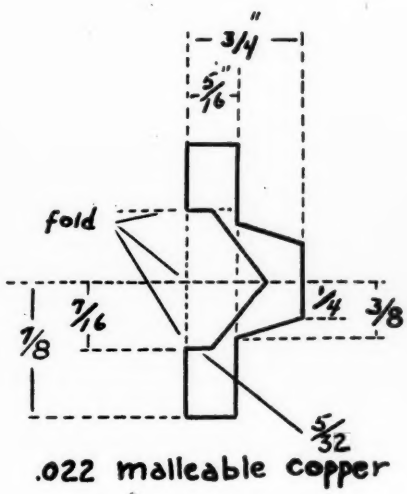

Figure 1. *Construction of Copper Base for Hubless Needle (Actual Size).*

the apparatus from malleable copper sheeting and No. 19 and No. 23 needles.

The hubless needle described offers the following advantages: a broad malleable base, which may be bent to fit the contour of the infant's scalp or on occasion the dorsal finger vein of an older person; low inertia, making the needle difficult to dislodge; marked ease of insertion; and ease of observing back flow when the vein is entered.

A convenient method of assembly is to have the finished needle sterilized and wrapped, to have

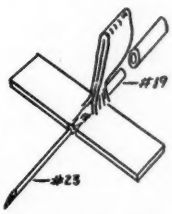

Figure 2. *Diagram of Hubless Needle and Base. The No. 19 and No. 23 needles are inserted one inside the other and then soldered in the V formed by the two sides of the base.*

polyethylene tubing with an internal diameter of 1 mm. (0.034 inch) stored in 1:1000 Zephiran solution and to use available conventional No. 19 needles as adapters to standard equipment for in-

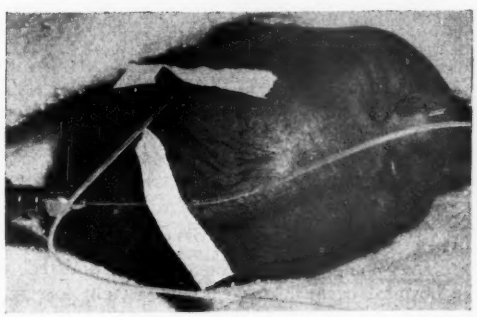

Figure 3. *Hubless Needle in Place. Note the ease with which blood may be seen when the vein is entered.*

travenous injection. After the component parts have been connected and the needle inserted, a single piece of tape, 13 by 51 mm., placed half on the copper base and half on the skin easily holds the assembly secure.

*Chief pediatrician, Hill Air Force Base Hospital, Hill Air Force Base, Ogden, Utah; formerly, pediatrician, Deaconess and St. Michael hospitals and Grand Forks Clinic, Grand Forks, North Dakota.

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CHERCHEZ LA FEMME

THE following letter, penned in Lebanon on April 19, has been going the rounds since its arrival in this country. From the American Psychological Association, Inc., to which it was directed, it was referred on April 30 to the American Psychiatric Association and from the American Psychiatric Association some three months later to the Boston Society of Psychiatry and Neurology. Local inquiries having failed to reveal the object of the quest, a reader into whose hands the letter finally came has solicited the aid of the *Journal* in the search.

Rue des Jesuites
Beyrouth, Lebanon

Dear Sir,

I am indebted for your address to the United States information service in Beirut. I wish to ask you the following service.

Last summer, I met in Paris an American lady who charged me with different things which I fulfilled for her. Unfortunately I lost her address and all I know about her is that her name is "Miss Carolyn" and she works as a secretary to a well known psychiatrist in Boston.

I will therefore be very grateful if you will kindly publish the following notice in your review, or any other similar review published in Boston, if you deem it necessary.

"Miss Carolyn, secretary of a psychiatrist in Boston and who met in Paris, last summer, Me. L. Sabbagh, is kindly invited to write to him at the above address."

Yours very truly,
ME. LÉON SABBAGH

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38511

PRESENTATION OF CASE

A sixty-four-year-old woman was admitted to the hospital because of weakness, weight loss and jaundice.

The patient had been followed in the Out-Patient Clinic for the past fifteen years because of hypertension — blood pressure of 188 to 260 systolic and 90 to 140 diastolic — for which she was treated with a regimen of weight reduction and Luminal tablets. Two or three years before entry she began to experience squeezing pain in the anterior portion of the chest that lasted three to five minutes and was brought on by exertion, accompanied by sweating and relieved by rest. These attacks continued until thirteen months prior to entry, when she had the onset of severe substernal squeezing pain radiating to both arms, lasting two or three hours, relieved by morphine and accompanied by weakness, hypotension, sweating and a feeling of impending doom. Her physician treated her with "small pills" and kept her in bed for twenty-one days, during which she was orthopneic for the first time. Since that time, the patient had dyspnea on exertion, orthopnea requiring one or two pillows for relief and one or two attacks of paroxysmal nocturnal dyspnea but no peripheral edema. After this episode she was gradually ambulated but was unable to regain strength, and for the ten months before entry had increasing weakness, anorexia, malaise without fever and a weight loss of 20 to 40 pounds. The blood pressure was considerably lower than before.

For the preceding seven months she was aware of epigastric fullness with a feeling of pressure and dull aching made worse by eating. This was accompanied by belching, nausea and occasional vomiting, with increasing anorexia for the past three months. During all this time she was followed by her physician, who noted a large liver but apparently no other masses or other evidence of liver disease. Two days before admission he observed jaundice for the first time. There had been no pain in the chest similar to the severe attack that occurred thirteen months before admission, although more recently she had pain in the right side of the chest made worse by breathing. There was no history of alcoholism, exposure to toxic substances, melena, hematemesis, back pain or change in bowel habits. Iron pills had been the only medication for the six months before entry.

Physical examination disclosed a pale, icteric woman who appeared to have lost weight recently. There was funduscopic evidence of arteriolar narrowing, with arteriovenous nicking and small exudates bilaterally in the macular region. The neck veins were flat. There were rales at both lung bases, with decreased breath sounds, resonance and tactile fremitus at the right base. There were scattered rhonchi with harsh breath sounds anteriorly. The

heart was enlarged, the border extending 2.5 cm. to the left of the midclavicular line. The rate was irregular because of multiple premature beats. There was a diastolic gallop rhythm, and the pulmonic second sound was greater than the aortic. A Grade 2 systolic murmur was present over the apex. The lower border of the liver was palpable 5 fingerbreadths below the costal margin and slightly tender. A large, tender mass, which moved with respiration, was palpated in the mid-epigastrium by some observers at times; however, the mass was usually absent. There was a question of a small mass high in the right vault on rectal examination. Bilateral mild varicose veins and clubbing of fingers and toes were noted.

The temperature was 99°F., the pulse 100, and the respirations 20. The blood pressure was 130 systolic, 90 diastolic.

The urine was dark amber, had a specific gravity of 1.028, gave a ++ test for bile, a ++ test for albumin and a negative reaction for sugar, and contained 1.2 Ehrlich units of urobilinogen per two-hour specimen. The sediment was bile stained and contained 20 white cells and an occasional red cell per high-power field. Examination of the blood revealed a hemoglobin of 12 gm. and a white-cell count of 12,600, with 88 per cent neutrophils, 6 per cent lymphocytes and 6 per cent monocytes. Smear of the blood disclosed some variation in size and shape of red cells, with rare elongated and bizarre-shaped cells. The serum bilirubin was 2.9 mg. direct and 4.4 mg. total, the alkaline phosphatase was 10.3 mg., the total protein 6.14 gm., the albumin 3.66 gm., the globulin 2.28 gm. and the nonprotein nitrogen 22 mg. per 100 cc. The prothrombin time was 16 seconds (normal, 13 seconds), and the cephalin flocculation ++ in twenty-four and forty-eight hours. The blood Hinton test was negative. A stool was negative for occult blood. A roentgenogram of the chest showed moderate elevation of the right leaf of the diaphragm and slight nodularity of the diaphragmatic contour bilaterally, more marked on the right. There was an irregular, mottled density throughout the right lung; the left lung was relatively clear except for some prominent vascular markings in the upper-lung field. The heart was greatly enlarged, showing prominence of the left ventricle. The costophrenic sinuses were clear (Fig. 1). On upper gastrointestinal series the esophagus appeared normal. There was a small hiatus hernia. No intrinsic lesion of the stomach, duodenum or upper jejunum was demonstrated, and the stomach and duodenum were displaced to the left by a large right abdominal mass that was thought to represent a greatly enlarged liver (Fig. 2). The duodenal loop was not widened. A cholecystogram was interpreted as showing a nonfunctioning gall bladder. No opaque stones were visible. An electrocardiogram revealed a normal rhythm, a PR interval of 0.14 second and occasional ventricular premature beats. The T waves were upright in Lead 3, low in Lead 2 and inverted in Leads 1, V_4, V_5 and V_6. The R waves were low to

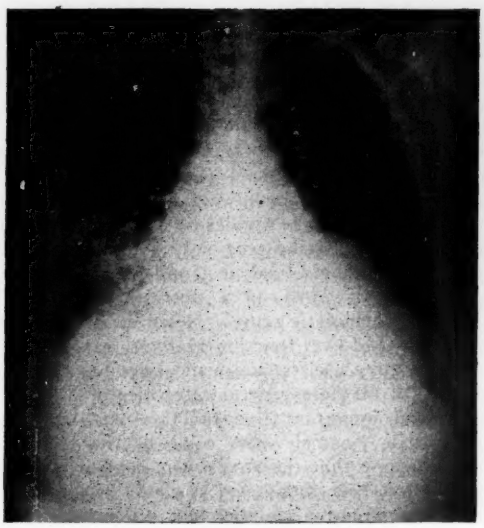

FIGURE 1.

FIGURE 2.

absent in Leads V_1, V_2 and V_3. The Q waves were deep, and the ST segments elevated in Leads V_4, V_5 and V_6.

In the hospital there was little change in the patient's condition, and on the fourth day an operation was performed.

Differential Diagnosis

Dr. Robert L. Berg*: There are two principal problems in this case: the cardiac situation, which, being of secondary importance, I think I shall deal with first; and the large liver. This patient with obesity had the ideal background for hypertension, which was demonstrated not only by direct measurement but also by the retinal changes. As a woman with hypertension, she had the proper background for angina. About a year prior to entry she had a thrombosis apparently and almost certainly a sizable infarct because the blood pressure remained much lower thereafter. As a secondary consequence of infarction congestive heart failure developed. The neck veins were described as flat, and she had no peripheral edema, but the evidence for left-sided failure is considerable even without the orthopnea that occurred shortly after the infarction — for she had dyspnea, bilateral rales and an irritable heart with a gallop rhythm. She apparently had no pleural fluid, and if we can rule out the liver, she had no right-sided failure, so the heart condition was not as advanced as I might have thought in view of the other findings. There was one finding about which I am uncertain — that is, the persistently elevated ST waves a year after infarction. If during the period of observation the ST waves returned to normal and were only recently elevated again, the diagnosis would be another infarction, in spite of the lack of a clinical story for it, but if they remained constantly elevated or attained a plateau level relatively soon after the infarction, without intervening clinical evidence of further infarction, we must consider the possibility of an aneurysm of the heart.

Now I come to the succulent morsel in this case: the liver disease. First of all, there were a number of constitutional symptoms. Weakness, malaise, anorexia, nausea and some vomiting developed. As a result, I suppose, of those and other things, the patient began to lose weight; we know it was 20 to 40 pounds but we do not know how much of it was related to the disease and how much to weight-reduction regimen for the hypertension. Apparently, it was a good deal more weight than was expected because it is indicated that there was a change. The weight loss is important in this case, in which carcinoma is the principal suspect, because it lends considerable likelihood to such a diagnosis. She was pale; actually the anemia was slight — the hemoglobin was only 12 gm. She had clubbing, which could have been associated with either the pulmonary lesion, which appears to have been an infiltration in the right lung, or the liver disease itself. Certainly, clubbing is not uncommon in cirrhosis, particularly of the intrahepatic biliary obstructive type, but it may be seen with any type of cirrhosis. I should also refer to the red-cell changes as probably constitutional changes inasmuch as they were the indirect result of involvement of either the stomach or the liver. I do not know much about their shapes except that they were bizarre; they might have been the burr cells seen in carcinoma of the stomach or the target cells or the Mexican-hat cells seen in liver disease with or without jaundice. Finally, the white-cell count of 12,600, with 88 per cent neutrophils, could have been due to inflammation or to necrosis within a cancer. This completes the constitutional findings, and now I come to the local findings.

The patient had a digestive disturbance, either a long process of intrinsic gastrointestinal disease within the gut itself or perhaps invasion from a pancreatic tumor. However, one of the mysteries of liver carcinoma is that it causes precisely such disturbances without actual mechanical interference. Moreover, she had serious liver trouble. First of all, the liver was very large. If she had had fluid in the right side of the chest or in the abdomen, the size of the liver would have been difficult to determine; since fluid was not present, it was a very large liver.

Secondly, she had jaundice and was pale without much anemia, so I wonder if the predominant feature was that she was only jaundiced. Traditionally, I should analyze jaundice on the basis of whether it arose from obstructive liver-cell damage or hemolytic causes. However, in this case all the tests of liver function were in a range where they are quite useless, and could have been due to any or all of these general categories of disorder. The most important liver-function test was not mentioned, — namely, the color of the stool, — but I assume that the stools were colored or they would have been mentioned as clay white. Therefore, if obstructive jaundice was presented it was not complete. I cannot rule out hemolytic jaundice on the basis that the urine urobilinogen was not markedly elevated because with a minor hemolytic process there may not be large amounts of urobilinogen in the urine. Possibly, there were elements of all three.

The next localizing finding is the pleurisy in the right chest, which apparently was prominent; furthermore, there was infiltration in the lung so there was definitely an abnormality in the right side of the chest.

The fourth finding of localizing importance is the epigastric mass, which apparently was felt by some of the observers some of the time but not all the observers all the time. I therefore do not think we need consider it a fraudulent observation.

*Assistant physician, Massachusetts General Hospital.

As a matter of fact I do not have much sympathy for the point of view that one either does or does not feel something. There is, between the area of absolute certainty of feeling or seeing and not feeling or seeing various physical signs, a vast area in which one would certainly undertake at great risk to state that something definitely was or was not present. I think, inasmuch as some people felt it and some did not, I can only say that the evidence was so meager that we cannot be sure. It is, of course, important in terms of the site of a primary tumor, but the fact that it moved with respiration and that the gastrointestinal series was negative makes it appear very much as if it were the left or right lobe of the liver.

DR. DANIEL S. ELLIS: There were two masses: one was the liver, and one was the gall bladder. We could palpate the gall bladder bimanually; it was an inconstant finding; one day it was not palpable and another day it was.

DR. BERG: I thought the mass was in the epigastrium.

DR. ELLIS: It was the same mass that was felt.

DR. BERG: But not all observers felt it.

DR. ELLIS: Not only is it true that not all observers felt the mass, but the same observer could not always feel it. It was there sometimes and sometimes it was not, but I am sure that it was gall bladder.

DR. BERG: The other mass, which constitutes the last local finding, was in the right vault. It was questionable, however, and was felt apparently with no certainty. It may have represented a mass in the cecum; it may have been either feces or tumor. Perhaps it could have been related to the ovary. The question is whether the disease could have been anything but cancer. I think the lesions that were present — namely, infiltration in the lung, a large liver and a question of involvement of the diaphragm — certainly point to cancer rather than infection. There was not really very much to suggest infection that could be as widely distributed as this, and I shall disregard it. Furthermore, a cancer in the liver might result in all the changes and might give rise to obstructive jaundice, liver-cell jaundice and hemolysis. Certainly, the first two conditions result; hemolysis has been frequently noted lately in cancer. Before differentiating primary and secondary liver disease due to cancer, I should like to see the x-ray films. The first specific question I should like to ask is whether or not there is any evidence of an aneurysm of the heart.

DR. STANLEY M. WYMAN: The tremendously enlarged heart is well seen (Fig. 1). I think the enlargement is primarily of the left ventricle. The question of a cardiac aneurysm cannot be settled from these films alone although I do not see it on the films. Very commonly such an aneurysm is best seen with the patient turned in the right anterior oblique projection; it can be seen by the fluoroscopist or on appropriate films. The tortuous aorta can be visualized through the heart. The hazy mottled density throughout the entire right lung, which is described in the protocol, is visible. There is some engorgement of both hilar vessels, but it is not striking. The left lung shows no intrinsic abnormality. The right leaf of the diaphragm is quite elevated. I am not impressed by any nodularity, and I do not think the changes described in the diaphragm can be taken too seriously.

DR. BERG: Is there any nodularity of the posterior portion of the lateral part of the diaphragm?

DR. WYMAN: That portion, which is faintly seen in this film, I think, could be passed as normal.

DR. BERG: It is true that one does not worry much about nodularity of the anterior portion of the diaphragm, but in the posterior portion it may be significant.

DR. WYMAN: It may be important in any position, actually. I think it is a matter of interpretation. It is hard to be didactic about it. The two films taken from the Graham test show no contrast substance in the gall bladder, and presumably this is a nonfunctioning gall bladder. However if the patient had much jaundice one cannot assume that the gall bladder was diseased.

DR. BERG: Would you even consider in passing that the pulmonary infiltration might be vascular, or does it appear as an infiltration?

DR. WYMAN: I think it is outside the vessels in the pulmonary parenchyma itself; I think there is some change in the pulmonary vessels, however — some pulmonary engorgement.

DR. BERG: Does it look to you consistent with metastatic disease?

DR. WYMAN: I thought it might be pulmonary edema.

DR. BERG: Do you often see pulmonary edema this much localized?

DR. WYMAN: This is not common, but it definitely occurs.

DR. BERG: Would you expect that there would be that much edema without fluid in the costophrenic sinus?

DR. WYMAN: I should like to see fluid in the costophrenic sinus, but that does not deter me from making the diagnosis of pulmonary edema.

DR. BERG: Does it appear unlike metastatic disease?

DR. WYMAN: I think the disease is too widespread and too confluent and lies perhaps in not as stringy and linear a fashion as lymphatic spread of metastases; it is not as discrete and nodular as it usually is with nodular metastases.

DR. BERG: Do you have anything to say about the mass in the abdomen? Does it appear to be entirely liver, or can you see two masses?

DR. WYMAN: I cannot outline a mass. I see only an apparently normal stomach and duodenum

greatly displaced by the large liver, which seems to extend down to the iliac crest (Fig. 2). I wonder if there is pressure by an enlarged common duct on the duodenum at the junction of the first and second portions.

DR. BERG: What is the difference in the density in the right upper quadrant?

DR. WYMAN: I think that is an artifact. I think it is probably soft tissue in the chest or abdomen.

DR. BERG: You would not care to make a diagnosis of hemochromatosis on the basis of that?

DR. WYMAN: I would not.

DR. BERG: That is very confusing. Actually, metastatic disease to the lung is not often so well localized as this. In view, however, of the helpful comments, I am somewhat tempted to abandon my original diagnosis, which was a hepatoma of the liver, because that diagnosis depended to a large extent on the evidences of local involvement. Certainly, if I were able to put any faith in the irregularity of the diaphragm, hepatoma would be a most attractive diagnosis, and if the spread in the lungs had been lymphatic in nature, it would be more tempting because of the common tendency of this tumor to metastasize, in a sense, locally. Inasmuch as pleurisy was also present, there seems to have been pleural involvement by some such disease. Of course if that were cancerous involvement I should be disappointed not to see fluid in the costophrenic angle also. The suggestion then arises, since Dr. Ellis pointed out that there was a palpable gall bladder, that this was due to carcinoma of the pancreas, with obstruction and probably with metastases to the liver. I do not believe this large liver would have resulted from obstruction alone without more jaundice. And the pulmonary picture then would be due to left-sided congestive heart failure. However, I must confess that I am not really happy about this diagnosis either; it is very much of a toss-up in my mind whether to choose primary liver cancer or carcinoma elsewhere in the abdomen obstructing the common duct. I think I shall select primary hepatoma simply because I have been wrong more often the other way than this way.

DR. BERNARD M. JACOBSON: What about a common-duct stone, Dr. Berg?

DR. BERG: I do not think she would have had as large a liver from a common-duct stone without more jaundice. Furthermore, she should not have had so much color in the stool. It seems to me that the liver would not have been so large with a common-duct stone that was not completely obstructing.

A PHYSICIAN: Would you consider a gall-bladder cancer?

DR. BERG: That gall bladder bothers me, I must confess, but because it was not universally accepted as being palpable I believe that there is a way out.

DR. ALLEN G. BRAILEY: Would you toy with the idea that it might have been pulmonary infarction?

DR. BERG: I think the jaundice could have been due to that, but I do not think the large liver could have been.

DR. BRAILEY: Might not the large liver have been due to congestive heart failure?

DR. BERG: The liver is large for congestive heart failure without peripheral edema.

DR. BENJAMIN CASTLEMAN: Dr. Ellis, would you tell us your opinion up to the time you operated on the patient?

DR. ELLIS: There was no question in my mind when I saw the patient, listened to her story and felt her abdomen that she had cancer of the liver or pancreas with metastases to the liver. In that way one could explain the palpable gall bladder. I was not impressed by any evidence of congestive heart failure. When I first saw her she had a few rales in the right lung but nothing more than that. She had no distention of neck veins and no peripheral edema. I might say that everybody did not feel as strongly as Dr. Wyman did that there might be congestion in the lungs because the x-ray report in the record is that the findings were consistent with lymphatic spread of metastatic tumor in the lungs. Perhaps Dr. Wyman was influenced by some films that he has not yet shown us.

CLINICAL DIAGNOSIS

Carcinoma of pancreas, with metastases to liver and lung.

DR. BERG'S DIAGNOSIS

Hepatoma, with metastases to lung.

ANATOMICAL DIAGNOSIS

Chronic passive congestion of liver.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Dr. Ellis did an aspiration liver biopsy believing that perhaps this patient was not well enough to be explored. The biopsy showed something we do not ordinarily see in a liver biopsy — markedly distended, blood-filled sinusoids and nothing else. In other words we have an example here of congestive heart failure with severe chronic passive congestion in the liver. When we usually see this condition in the autopsy material the sinusoids are not so distended. One can easily understand how in the active liver these tremendously dilated sinusoids can press against some of the bile canaliculi and produce insufficiency. Table 1 is from a paper by Sheila Sherlock,* of London, who I believe is the first person to record a series of aspiration liver biopsies on patients with congestive heart failure and compare them with the

*Sherlock, S. Liver in heart failure: relation of anatomical, functional and circulatory changes. *Brit. Heart J.* 13:273-293, 1951.

amount of bilirubin in the serum. It will be noticed that the bilirubin is higher in the cases with the more severe liver disease and still higher if associated with pulmonary infarction. I believe the case under discussion would fit in with Group A liver disease, because there was not much necrosis in the central areas — merely congestion.

One might ask, How are we sure that this patient does not have cancer? Perhaps Dr. Ellis can continue from there.

DR. ELLIS: After we looked at the liver biopsy we treated the heart failure more intensively with mercurial diuretics in addition to the digitoxin. Immediately, the mass that we had been feeling in the liver began to shrink in size, and the jaundice began to disappear. The patient was discharged from the hospital twelve days after the liver biopsy clinically much improved. She had some subsequent chest films, one done as I remember four or five days later and one on the day she left the hospital that Dr. Wyman will interpret for you. I saw her in the office two months after the operation, when the serum bilirubin was normal, the liver edge was only two fingerbreadths below the costal margin and she was walking around and had not gained any weight. I am still not sure that she does not have a ball-valve stone in the common duct, but at present she is improving — the jaundice is all gone — so I am going to play it that way for a while.

DR. WYMAN: The films of the chest taken after operation show definite improvement, with clearing of the process in the right lower lobe; this, of course, is much more consistent with clearing of pulmonary edema or resolution of consolidation than with partial disappearance of tumor. The heart shadow has definitely decreased in size during the course of the postoperative x-ray examinations (Fig. 3).

DR. CASTLEMAN: I should think the fact that the pulmonary process disappeared so rapidly would be more in favor of congestion and edema than infarction although there may have been a small infarct that resolved fairly well. Do you see any white lines of scarring as a result of the healing?

DR. WYMAN: I looked for infarcts in this patient, but I could not find any. In answer to Dr. Ellis' question, it is perfectly true that I had all the films, and, of course, that influenced me tremendously. I wanted to give Dr. Berg the benefit of that if I could.

DR. BERG: I did not make good use of it.

DR. WYMAN: To go back to the original films, I believe that there is unlikely to be this much metastasis in one lung and nothing in the other; that is a much more common picture with congestive changes and edema. Underlying infarction is a real possibility and may never be discovered by x-ray examination.

DR. BRAILEY: Is there still digestive distress?

TABLE 1. *Serum Bilirubin in Relation to Liver Histology in Patients with Cardiac Failure.*

No. of Patients	Mean Serum Bilirubin	Grade A Liver Disease		Grade B Liver Disease		Grade C Liver Disease	
		No. of patients	Mean serum bilirubin	No. of patients	Mean serum bilirubin	No. of patients	Mean serum bilirubin
	mg./100 cc.		*mg./100 cc.*		*mg./100 cc.*		*mg./100 cc.*
Without pulmonary infarction:							
28	1.4	11	0.9	10	1.6	7	2.1
With pulmonary infarction:							
14	3.2	3	2.6	4	3.1	7	3.5

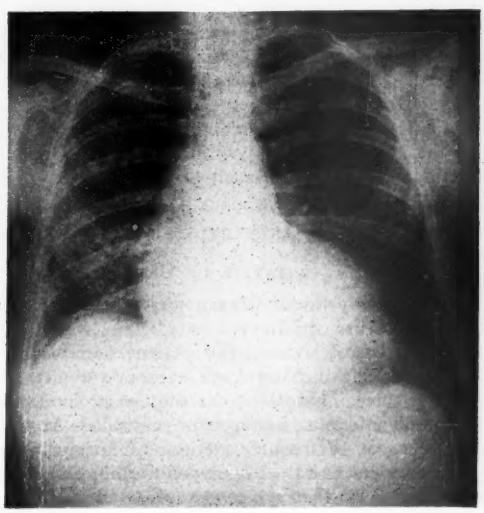

FIGURE 3.

DR. ELLIS: The patient has a good appetite, but she is still not gaining weight.

DR. BERG: How about the clubbing?

DR. ELLIS: She still has the clubbing.

A PHYSICIAN: How do you interpret the electrocardiogram?

DR. ELLIS: As evidence of old anterior infarction.

DR. BERG: How do you explain the continually elevated ST segment?

DR. ELLIS: The official opinion was "this is a classic pattern of rather large anterior myocardial infarction; it could be old or recent."

DR. STUART RAGLAND, JR.: How do you explain the palpable gall bladder, if that was what you felt?

DR. ELLIS: I cannot explain it, unless she had a stone in the cystic duct that dropped back. I do not see how you can explain that on the basis of congestion.

DR. CHESTER M. JONES: The Graham test showed a nonfilling gall bladder; I think it should be remembered that a bromsulfalein test on patients with large congestive livers and congestive heart failure often shows 30 or 40 per cent retention of the dye, which returns to normal when cardiac compensation is re-established. I should suspect that the Graham test followed the same pattern — that the dye did not get into the gall bladder in sufficient concentration to show filling and therefore a "nonfilling gall bladder" was reported. It is also possible that the patient had gallstones with cholecystitis, but it is more probable that the finding was due to impaired liver function.

DR. BERG: The moral of this case to me is that one can have an enormous liver in heart failure without peripheral edema. I think that is rather impressive.

DR. ELLIS: Yes; and she was lying perfectly flat in bed — preferred to lie flat rather than to be elevated. The failure certainly was right sided.

DR. JONES: In that respect, it is entirely comparable to adherent pericardium with a large liver, and the ability to lie flat without difficulty. Liver function is disturbed in such cases.

CASE 38512

PRESENTATION OF CASE

A sixty-five-year-old woman was referred to the hospital because of fatigue.

At the age of sixteen, the patient had become "anemic." She did not have excessive menstrual bleeding, bleeding from other sources or evidence of chronic infection; her appetite was good. At this time, because of frequent periods of fatigue, iron pills were prescribed, without definite improvement in symptoms. The symptoms recurred over the years, and the patient continued to take iron, stopping the pills when she felt better and starting them again whenever she felt tired. Twenty-four years before admission she was also advised to eat substantial quantities of liver. Two years later a hemorrhoidectomy and a tonsillectomy and adenoidectomy were performed in the hope that these procedures would alleviate the anemia. At the same time she began to receive "liver shots" every two weeks, which were continued up to the time of admission. She had continued to take iron during this time, and more recently, for an indefinite period, she had been on folic acid therapy. Seven years before entry gastrointestinal and gall-bladder series were negative. At this time all medication but the iron was stopped, after which the symptoms became worse. Four months before admission after a bout of diarrhea lasting two weeks, a physician found the liver to be enlarged.

The patient had had three uneventful pregnancies. She had noted some constipation while on iron therapy, but otherwise the systemic review was negative. Several friends had asked why her skin had grown darker; however, the patient had not noted any obvious change and thought she was "tan." She was an occasional drinker. She had not had any bleeding, weight loss, chills, fever or jaundice. Her appetite was considered adequate.

Physical examination showed a well developed woman with spotty, brown pigmentation of the skin of the face and arms; the pigmentation was increased in the creases of the palms. The mucous membrane of the mouth was not pigmented. No icterus was noted. There was a Grade 3 aortic systolic murmur radiating to the neck and a Grade 2 mitral systolic murmur. The aortic second sound was greater than the pulmonic. The edge of the liver was tender and was felt 5 fingerbreadths below the costal margin. The tip of the spleen was palpable.

The temperature was 98.6°F., the pulse 90, and the respirations 20. The blood pressure was 170 systolic, 84 diastolic.

The urine had a specific gravity of 1.025 and showed a slight trace of albumin but was negative for sugar. The sediment contained 6 white cells, a rare red cell and 3 hyaline casts per high-power field. Examination of the blood revealed a hemoglobin of 11.2 gm. per 100 cc. and a red-cell count of 3,300,000. On smear the red cells were achromic and varied in size, and the platelets were decreased. The white-cell count was 6900, with 71 per cent neutrophils, 23 per cent lymphocytes, 1 per cent eosinophils, 1 per cent basophils and 4 per cent monocytes. The MCV (mean corpuscular volume) was 100.9 cubic microns (normal, 80 to 94 cubic microns), the MCH (mean corpuscular hemoglobin) 30.7 micromicrogm. (normal, 27 to 32 micromicrogm.), and the MCHC (mean corpuscular hemoglobin concentration) 31.2 per cent (normal, 33 to 38 per cent). The prothrombin time was normal, and the sedimentation rate was 18 mm. in one hour. The alkaline phosphatase was 1.8 units, the total protein 6.25 gm., the albumin 4.40 gm., and the globulin 1.85 gm. per 100 cc. A glucose tolerance test was reported as follows: fasting sugar, 90 mg., half hour, 186 mg., one hour 182 mg., two hours, 101 mg. and three hours, 90 mg. per 100 cc. A bromsulfalein test showed 8 per cent retention of the dye. The urinary urobilinogen was 1.0 Ehrlich units. One stool specimen gave a positive guaiac reaction; three others were negative. Gastrointestinal and gall-bladder series done at

another hospital a month before entry were reported as negative.

On the second hospital day an operation was performed.

Differential Diagnosis

Dr. Bernard M. Jacobson*: The patient had taken iron by mouth for about fifty years and liver extract intramuscularly about every two weeks for approximately twenty-two years. What was the anemia that this patient had? Was she chlorotic at the age of sixteen? There was no mention of a green color, no anorexia and no apparent dramatic response to iron. In view of the type of blood picture later on, I should suspect that she had a low-normal hemoglobin, which is not uncommon in women, a condition that is sometimes called "congenital hypoplastic anemia," consisting of a life-long rather low hemoglobin with little change in the individual red blood cells. That condition is compatible with a long and useful life and is often seen together with a neurasthenic constitution. I should guess that the previous blood picture and the previous reason for iron administration had no relation to the present illness.

I should like to know about the menstrual history: she had three pregnancies, so at least she did not have amenorrhea. I am not told when she had the menopause — when she ceased to lose blood; I assume that it was at least twenty years before admission, at the age of forty-five. Was she drinking more than an occasional amount of alcohol? The large liver was of at least four months' duration. Was this just a low liver edge or a slightly enlarged liver with a low upper border? Was there any pigment in the axilla?

Dr. Chester M. Jones: The upper border of the liver, by percussion, was in the fourth interspace.

Dr. Jacobson: That is a large liver indeed.

Presumably, the operation that was performed on the second hospital day was a biopsy of some sort, and I suspect it was a skin biopsy; I do not think she had enough preparation for a liver biopsy.

There is no question that this patient had hypertension, probably hypertensive heart disease and probably aortic roughening. The aortic second sound was well preserved; I do not suppose that she had aortic stenosis.

The specific gravity of 1.025 shows good renal function. The blood seems to have been normocytic and fairly normochromic, with not too much anisopoikilocytosis — in other words, a nonspecific blood picture. The leukocytes were well preserved. I am uncertain how much significance to attach to the statement that "the platelets were decreased." One might conceive of a hypersplenic phenomenon, a large liver and a large spleen with thrombopenia, but I doubt that. I get no help whatever from the Wintrobe indexes. It is interesting that all the chemical determinations of liver function were apparently normal. I am not told about the bilirubin; I assume that the patient was not jaundiced.

In the presence of pigmentation, hepatomegaly, mild splenomegaly and only mild nonspecific anemia, with fairly good liver function, a few conditions bear consideration. If I look at the pigmentation alone, from the description in this record I do not see how I can make any diagnosis. Addison's disease is certainly well ruled out by the good nutrition, general good appetite and hypertension. This does not look like the distribution of the pigment of acanthosis nigricans. Since I am not told about any bluish tinge to the pigment, I shall discount such things as argyria, bismuth intoxication or chronic arsenic poisoning. There is one form of pigmentation that is not usually considered. This is produced by certain sun creams that women use on their faces and on their arms, which, in the course of use, get in the creases of their hands and which, when exposed to the sun, cause pigmentation or tanning. That possibility is something I cannot rule out.

The trap that apparently has been set for me is hemochromatosis. The description is not that of the bluish-gray pigmentation of hemochromatosis; it is brown. In color it fits the pigmentation of Addison's disease. The patient had been taking iron most of the time for fifty years, and pigmentation and a palpable liver and spleen had developed. On the other hand, there are some important reasons why this was not a case of hemochromatosis. In the first place, she was a woman; about 90 cases out of 100 are in male patients. The few women in whom it does occur almost all have an abnormal menstrual history. They do not bleed enough. This patient had had three children; hence she must have had a good menstrual history. The pigmentation was brown instead of bluish gray. Diabetes was absent; in 75 per cent of the cases there is diabetes or a glucose tolerance test suggestive of diabetes. In the few cases of proved human hemochromatosis related to increased absorption of ingested inorganic iron, the diagnosis has been an extremely bizarre one indeed. The absorption of inorganic iron in a normal person on a normal diet is usually considered to be too low to produce hemochromatosis. A woman who menstruates properly, by her monthly mild bleedings, is protected against hemochromatosis. This patient certainly had not been on the deficient diet described by Gillman and Gillman[1] in South African natives who develop hemochromatosis.

Looking at the liver and spleen per se, I must rapidly go through the usual motions. Was this congestive heart failure with splenomegaly and hepatomegaly? There was no evidence of heart failure, and one sees splenomegaly only in late cardiac cirrhosis. Was there an infiltration of metastatic carcinoma in the liver? I should say

*Assistant physician, Massachusetts General Hospital.

that the splenomegaly is against that. Did she have sarcoidosis or Hodgkin's lymphoma. I do not think we can rule that out completely.

Although the gastrointestinal series was negative, I do not believe that rules out esophageal varices. This picture of a woman, who had diarrhea a few months previously, a mild anemia and at least one positive stool guaiac reaction, I think, best fits a mild, functionally intact, early idiopathic portal cirrhosis, with mild portal hypertension. My diagnosis of the pigmentation is uncertain. I should say that the patient had hypertension, hypertensive and arteriosclerotic heart disease, portal cirrhosis and skin pigmentation of uncertain origin.

Dr. Perry J. Culver: I should like to disagree with the statement that the bromsulfalein retention of 8 per cent was normal. I think that with a mild degree of anemia 8 per cent probably represents an abnormal degree of retention. The glucose tolerance test of 182 mg. per 100 cc. at one hour is a little suggestive of diabetes. The pigmentation that is described might have been associated with cirrhosis. We have seen a number of cirrhotic patients who had pigmentation not unlike this.

Dr. Jacobson: Yes; I meant to mention that nonspecific pigmentation might go along with the cirrhosis.

Dr. Thomas Hall: I should like to mention a study from the medical service of the Peter Bent Brigham Hospital recently performed on the amount of hemochromatic pigment analyzed photometrically. Two male patients had hemochromatosis of long standing, with saturation of the iron-binding globulin and with testicular atrophy; they showed on photospectrometry of the skin a picture that was not characteristically different from that found in Addison's disease except for the fact that they had some castrate findings of low blood flow so we saw no characteristic blue in these 2 proved cases at all. The pigmentation, as far as we could tell clinically, was exactly analogous to that of Addison's disease, and as far as we could tell spectrophotometrically it merely had an additional component of decreased oxygen saturation and diminished blood flow to the skin. There was no specific pigment. This is in keeping with the description of the pathological findings as given by Jeghers,[2] who showed a great melanin concentration in the corium and a variable amount of iron pigment.

Dr. Benjamin Castleman: In the skin of most patients with Addison's disease that we see microscopically we do not find iron, but we do find iron in the corium in cases of hemochromatosis. Microscopically, we can certainly tell the difference if it is positive even if you cannot with the use of the spectrophotometer.

Dr. Hall: I meant that clinically it is not possible to make a differentiation.

Dr. Castleman: Yes; it is quite possible that the iron seen in the skin of the patient with hemochromatosis has nothing to do with the clinical appearance of the skin itself. That may be due to the melanin.

Dr. Hall: Increased melanosis is due to the deposition of iron granules.

A Physician: Was the serum iron determined? Is there any report of hemochromatosis caused by oral administration of iron?

Dr. Jacobson: I have not run across any case in which oral ingestion of iron produced hemochromatosis. In a series of 23 cases of hemochromatosis, studied by Althausen and his co-workers[3] in Australia, there was not a single instance of iron ingestion.

A Physician: Do people with prolonged hemolytic anemia develop hemochromatosis?

Dr. Jacobson: They develop hemosiderin deposits, but they do not develop the full-blown picture of hemochromatosis.

Dr. Castleman: I think that is true. In hemosiderosis iron is found in the liver, primarily in the liver cells and the reticuloendothelial system, but not in the stroma of the portal spaces nor in the bile-duct epithelium such as is seen in hemochromatosis; it may be seen in other organs of the body such as the spleen and lymph nodes.

A Physician: Might this case not have been one of hemolytic anemia?

Dr. Jacobson: From the data available there is no evidence of hemolytic anemia in all these years.

Dr. Castleman: Dr. Jones, would you tell us about the patient up to the time of the biopsy.

Dr. Jones: When she came in, the first important thing was to see whether the anemia was due to bleeding from the gastrointestinal tract. In her home town, studies had been done that seemed to rule out such a possibility; those studies were confirmed here. There was no evidence of bleeding at any time. The large liver was the obvious thing that had to be explained. The pigment was not diagnostic, as Dr. Jacobson has pointed out, but it was certainly consistent with cirrhosis of the liver, with hemochromatosis and with some wasting disease that she did not have. Since we have had several cases of hemochromatosis in which skin biopsies have failed to show the iron-containing pigment, it seemed to me that a skin biopsy was not the best method of establishing the diagnosis. The quickest way to make a diagnosis was to look at a piece of liver, because I think we have never failed to make a diagnosis in cases of hemochromatosis by this means. The patient was properly prepared for biopsy. The prothrombin time was normal; she was put on vitamin K a day or two before biopsy; and the biopsy was done without incident.

DR. JACOBSON: Had I known this was your patient, I should have said the biopsy was from the liver.

CLINICAL DIAGNOSIS

?Hemochromatosis.

DR. JACOBSON'S DIAGNOSES

Portal cirrhosis, idiopathic.
Hypertensive and arteriosclerotic heart disease.
Skin pigmentation of uncertain origin.

ANATOMICAL DIAGNOSIS

Exogenous hemochromatosis due to iron ingestion.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: In this iron stain of the liver biopsy one can see the iron within the liver cells. If we saw this picture alone, we could not rule out merely hemosiderosis. The next slide shows a definite cirrhosis, with large amounts of connective tissue in the portal spaces; in this island, which is all a portal space, one sees all the iron deposited in the portal areas, in the stroma and within the bile-duct epithelium, which is the picture that the pathologist calls hemochromatosis rather than hemosiderosis.

We were much intrigued, as Dr. Jones and Dr. Jacobson were, with the idea that this might perhaps be an exogenous type of hemochromatosis. Exogenous hemochromatosis has been described after numerous transfusions[4] but rarely if ever after oral ingestion of iron. Wallerstein and Robbins[5] recently described a patient, similar to the patient under discussion, with congenital hemolytic anemia who received iron for fifteen years. Although their patient, also a woman, did have congenital hemolytic anemia, they believed that the amount of hemosiderin deposits could not be entirely due to hemolytic anemia, and since they estimated that the iron intake was great, they thought it must be due to the exogenous iron and that the factor of hemolysis might have aggravated the element of hemochromatosis. They also stated that perhaps there should not be a sharp differentiation between hemosiderosis and hemochromatosis — that perhaps hemosiderosis goes on to actual hemochromatosis. In their case the patient had diabetes and had hemosiderin deposits in many organs of the body, which would certainly be true of a case of hemochromatosis.

DR. JONES: The serum iron in the case under discussion today was about 350 microgm. per 100 cc., but that was reported subsequently.

DR. JACOBSON: Was the menstruation normal?

DR. JONES: As far as I know it was. Her nutrition had been good for years. There was nothing very abnormal in the picture except the long history of anemia, the iron administration and the large liver.

Her sister, one daughter and possibly a granddaughter had a queer anemia of many years' duration.

DR. JACOBSON: Was the patient of Mediterranean stock?

DR. JONES: No.

DR. CASTLEMAN: It is possible that there was a mild degree of hemolysis in this patient; certainly that in itself would not produce this picture in the liver. Perhaps the exogenous form of hemochromatosis was due to the combination of the two.

DR. JONES: I have just received a note from her doctor, who writes as follows regarding her lifetime consumption of iron:

> She was taken out of school at the age of sixteen for two years because of anemia and "incipient TB" (?). During this time she received 3 Blaud's pills a day. During her 3 pregnancies she always took iron, and she thinks the preparation and dose were the same. From the age of thirty-three to forty-two she was under the care of a physician who gave her iron pills and for a brief time injections of iron. I first saw her in 1932, when she was forty-four years old. For four years she took Blaud's pills, 6 a day for the first year and subsequently 3 pills a day as well as a crude liver extract. Four years later Feosol, 3 pills a day, was substituted for Blaud's pills. Iron therapy was discontinued six months before she was admitted to the hospital, and she was continued with liver extract and vitamin B_{12}.

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A MATTER OF FAITH

To many people in sundry areas and countries of the world, Christmas, with all the various interpretations and forms of observance that have grown up about it, typifies the very core around which faith is built. Its implication is that of a universal spiritual goal and a constant longing for that goal on the part of all socially conscious men and women.

Despite the failures of the past and the uncertainties of the present, it is significant that this faith can still annually renew for such persons the conviction of a brighter and more settled future. Such confidence can be maintained at this season without inconsistency by all persons of good will, indifferent to the details of race or religion. For it is necessary that all, according to their customs and institutions, must have faith in some higher security than any worldly power can guarantee.

It is significant that the Protestant churches of this area have this month united in a Festival of Faith, in a week given over to the reaffirmation of their belief in the ultimate morality of mankind; it is not inconceivable that a similar expression of a still broader faith may eventually unite all people who believe in a spiritual authority greater than themselves, whatever the circumscribed teachings of their various creeds may be.

There must become current a more comprehensive and more universally accepted concept of faith than can be found within any single religion however widespread. It must be a concept that will put its entire emphasis on the ultimate attainment of a mutual belief in right thinking and right living, and in man's progress toward the stabilization of his global occupancy. It will accentuate good will toward man by all men of good will as common to all forms of worship and to all beliefs.

It is the message that is heard most clearly at Christmas time, and that can be accepted by all persons of any faith who believe in a brotherhood of man.

TECHNOCRACY, INDEED

TWENTY years ago, when man's inspired acquisitiveness had brought him to his lowest economic pitch in modern times, and the gold standard had received the blow from which it has never recovered, a new form of government was devised (at least on paper) that was to redeem the world for all mankind — or for that part of it that had accepted the belt transmission of power as a prelude to mass production. This was technocracy, or government by technical experts, possessed, at least in theory, not only of productive skills but of wisdom in their use — not only of the knowledge of how to make goods but of how much of them to make, and when and where. Thus the world would have achieved its first government by sheer intellect — if only by a certain type of intellect.

The fate of the resultant society of robots would have had its interest for those who care to contem-

plate such things, although certain observations indicate that a familiarity with machinery and the philosophy of its use do not necessarily go hand in hand, nor do more than a few men of science possess the knowledge of putting their science to the best use of mankind. Each generation may produce a few Leonardos, but it is questionable whether there are enough to have a whole system of government built up of them — and certainly not at the present rate of government employment. The intellectual capacity needed would be attributable to real scientists — not to the technologists out of whom the technocrats would have to be fashioned.

The course of this society might be forecast, in fact, by taking a slight liberty with one of Goldsmith's better known couplets:

> Ill fares the land to hastening ills a prey,
> Where men push buttons while their minds decay.

Nowhere does this hint of intellectual disaster find clearer expression than in the writing racket, where the most lasting results have been manufactured with the simplest tools. This has been noted for a long time, some of the finest literature since the hammer and chisel went out of date having been produced with the quill pen, a slowly moving vehicle of expression that allowed its user's thoughts to mature while the point was being whittled with a penknife.

The revolutionary steel pen, requiring only to be dipped and occasionally wiped, permitted the more rapid recording of a swifter train of thought and a consequent change in style, to be further modified by the ready flow of the fountain pen and finally by the typewriter. This instrument, whether employed by the author or by his shorthand amanuensis, has created a completely new style, except where it has been responsible for the complete abandonment of all style. One need not even mention the treachery of the electric machine, with its capacity for concealing the lowliest in slovenly diction behind a façade of the loveliest in modern lettering.

"Easy writing," as Thackeray — or others — once said, "makes damned hard reading," and many editors no doubt must be impressed by the overwhelming ease with which so many writers of learned papers have apparently tossed off their verbal thunderbolts, sheet after sheet. When even the technologic opportunities for good transcription are ignored, however, and smudged carbon copies of single-spaced typescripts are submitted in the vain hope of publication, one may wonder indeed what our literature is coming to (to what our literature is coming).

INTER-AMERICAN CENTER OF BIOSTATISTICS

In Santiago, Chile, the Inter-American Center of Biostatistics was established this summer, with the aid of the United Nations and the World Health Organization and in agreement with the government of Chile. The United Nations and the World Health Organization are to provide technical assistance, administrative personnel and certain equipment and supplies, as well as grants for training, during five years for the development of this center. The objectives will be to organize and develop a long-term training center for Latin America on vital and health statistics; to set up government offices in Chile concerned with various aspects of vital records and health statistics; to devise records and methods particularly applicable to Latin American countries; and to demonstrate a system of co-ordination among the central statistical, public-health and social services and other agencies. The schools of Public Health and Medicine of the University of Chile and the governmental departments of Statistics and Public Health and other appropriate agencies are the participating organizations of the Center at first, but provision is made for the participation of other agencies and other governments as may be deemed feasible.

This far-reaching, long-range project should provide the material for the development of a sound program of co-ordinated preventive medicine for the Latin American countries.

CHICAGO'S HOT RAGWEED

According to a press report emanating from the University of Chicago, "hot" ragweed, home grown in the midway greenhouses, may make future hay-fever seasons less of an ordeal than those of today. Radioactive pollen will be used to find out experimentally what happens to the irritat-

ing allergen when it comes in contact with the sensitized cell of the wretched victim's mucosa.

The ragweed is grown in sealed containers containing radioactive carbon dioxide. The carbon dioxide is taken up by the leaves, and the tagged carbon in the gas is incorporated in all parts of the plant. Tagged pollens can be injected into laboratory animals or possibly into the subcuticle of hardy volunteers, who would, presumably, be willing to sniff innocuous amounts of the hot snuff and submit to Geiger-counter counts between and perhaps even during sneezes and nibbles of antihistamines. The nature of the antigen-antibody explosion might be exposed, and knowledge gained from these experiments might aid physicians in eliminating that "sudden, noisy, spasmodic expiration through the nose," as the humble sneeze is defined by the new *Gould Medical Dictionary*.

PRIZE-ESSAY COMPETITION

The $100 prize-essay competition for fourth-year students closes March 15, 1953.

Full details were published in the *Journal* of October 16.

Drs. W. J. Mackarsie and Marshall Hall report, in the December No. of the London Lancet, a case of epilepsy cured by tracheotomy. We have several cases of the disease on hand, in some of which we intend to operate after the manner of Dr. Hall, and report results.

Boston M. & S. J., *December 22, 1852*

MASSACHUSETTS MEDICAL SOCIETY

BLUE SHIELD FOR PHYSICIANS

At its meeting in February the Council of the Massachusetts Medical Society will be asked to vote upon a number of controversial matters. One of these, which at first sight may not seem controversial at all, is whether or not the Society should sponsor membership for its Fellows in Blue Shield services.

There is probably not a physician who has not been the recipient of medical or surgical care for himself or his family from a fellow practitioner. Probably few if any medical men whose skill has been called upon in behalf of a fellow doctor or his family have felt any other emotion than a certain pride and gratification at being honored by such a request.

No one questions the fact that this arrangement is susceptible of abuse. A hypothetical well-to-do widow of a long-dead practitioner might, fifteen or twenty years later, demand and receive prolonged attention for a functional disorder although she could easily afford to pay for it. Or a son may require an appendectomy while hundreds of miles away from home in college, at the hands of an unknown surgeon who will never even meet the grateful father. One's wife, particularly if she has no financial worries, is embarrassed when her fourth or fifth baby is ushered into the world by a patient obstetrician whom she cannot reward with anything better than a few bottles of Scotch whisky that he does not want, or a gift to the hospital's outpatient department.

Such beneficiaries of professional courtesy are the chief advocates of Blue Shield membership for physicians and their families, especially if their husbands happen to be nonpracticing physicians who receive salaries just like other people. It would enable them to feel that the surgeon or physician can be paid for his sacrifice of time without embarrassment on either side.

But how about the younger men just starting out or some of the older ones who are marooned on the tiny rock of a limited retirement income, in danger of being swamped by the rising tide of increased living costs, to whom the Society-sponsored demand for an extra $35 is not easy to answer? They should not be made to feel obligated to join a group or to feel remiss if they do not do so.

Possibly Blue Shield membership should not be officially "sponsored," but merely made available if desired (group membership carries certain advantages over individual membership). Or perhaps fellows of the Society should continue to take out individual and family membership as at present, and forego the advantages of group membership.

A surgical consultant has suggested that members of the Massachusetts Medical Society might join the Blue Shield under Plan B, but when services are performed on physicians' families, the participating physician would accept Plan A payment for his services. This plan is probably not feasible under the present rules.

ROBERT W. BUCK, M.D.
Secretary pro tempore

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

ADMISSION OF ARTHRITIC PATIENTS TO LAKEVILLE STATE SANATORIUM

Provision for the admission of arthritic patients to the Lakeville State Sanatorium is provided by the addition of new legislation approved on June 25,

1952. This new amendment, Chapter 492, Acts of 1952, which was introduced by the New England Chapter of the Arthritis and Rheumatism Foundation, reads as follows:

Section 65A of Chapter 111 of the General Laws, as most recently amended by Chapter 412 of the Acts of 1948, is hereby further amended by inserting before the word "and", in line 4, the words: — or arthritis, — so as to read as follows: — Section 65A. The department may admit to the Lakeville State Sanatorium persons suffering from extra-pulmonary tuberculosis, persons crippled by poliomyelitis (infantile paralysis), or arthritis, and crippled children as defined in the regulations of the department; provided, that no person shall be admitted who has not been a resident of the Commonwealth for at least twelve months preceding the date of his application for admission, and that preference shall be given to citizens of the Commonwealth.

PHYSICIANS' REFERRAL. Arthritis patients who have lived one year or more in Massachusetts may be admitted by application of a physician to the Division of Tuberculosis, Room 546, State House, Boston, on forms provided by the Massachusetts Department of Public Health.

MEDICALLY INDIGENT AND INDIGENT PATIENTS. This unit is intended to supplement existing facilities for those patients unable to afford private hospital care. It is not intended that patients requiring only custodial care will be admitted.

TYPE OF TREATMENT. Complete facilities for treatment are provided. This treatment includes physical therapy, occupational therapy, and orthopedic surgery as indicated. At present, only 20 beds are available.

CORRESPONDENCE

NATIONAL HEALTH PROGRAM

To the Editor: In the "Secretary's Letter" of the American Medical Association dated September 24, 1952, there appear some inaccurate statements regarding the Committee for the Nation's Health.

On October 14, 1952, Mr. Leo Brown, director of the Public Relations Department of the American Medical Association, in a debate on National Health with Miss Helen Hall in Boston, made similar inaccurate statements.

The general trend of these statements is to attempt to smear the Committee for the Nation's Health with the taint of Communism. The attention of Dr. Louis H. Bauer, president of the American Medical Association, has been called to the inaccuracies in the statements of representative officials of the organization. It is hoped that he will see that these untruths, which have been widely distributed to the medical profession and to lay-groups, are corrected.

It is unfortunate that a subject so important and controversial as the development of a national health program is not debated on a high level of truth. It is particularly distressing to many members of the medical profession to have the officers of the American Medical Association employ smear tactics and perversion of the facts in discussions on a subject in favor of which millions of citizens have expressed themselves.

The following officers and directors of the Committee for the Nation's Health have full authority, and the only authority, for directing the policies of this committee:

Channing Frothingham, M.D.
William Green
Bishop Francis J. McConnell
Philip Murray
Bishop G. Bromley Oxnam
Mrs. Franklin D. Roosevelt
Gerard Swope
Walter Wanger
Morris Llewellyn Cooke
Walton Hamilton
Michael M. Davis
Viola W. Bernard, M.D.
James A. Brownlow
Paul B. Cornely, M.D.
John J. Corson
John Edelman
Abe Fortas
Frank F. Furstenberg, M.D.
Arthur Goldberg
Harry Goldblatt, M.D.
John Gunther
Henry Kaiser
Mary Dublin Keyserling
John A. Lapp
Joseph Meyer, M.D.
Newbold Morris
Dorothy Norman
James G. Patton
Eric Peterson
Jacob Potofsky
Harry Read
Emil Rieve
Samuel I. Rosenman
Theodore M. Sanders, M.D.
Max Seham, M.D.
Robert E. Sherwood
Boris Shishkin
Wayne Chatfield Taylor
Robert F. Wagner, Jr.
R. M. Walls, D.D.S.
Lester Washburn
Hubert Will
Wilson M. Wing, M.D.
Matthew Woll
John M. Brumm

A more loyal group of Americans, interested in national institutions, would be hard to find. To try by innuendo to persuade the public that these people are Communistic in philosophy or connections is an obvious deceit and unworthy of an organization that professes such high ideals as the American Medical Association.

I believe the time has come when the honorable members of the medical profession should protest against this method of approach to the discussion of a controversial subject by the officers of the Association.

CHANNING FROTHINGHAM, M.D.
Chairman

Committee for the Nation's Health
Boston, Massachusetts

BOOK REVIEWS

The Pathology of Diabetes Mellitus. By Shields Warren, M.D., Sc.D., and Philip M. LeCompte, M.D. Third edition. 8°, cloth, 336 pp., with 112 illustrations and 3 colored plates. Philadelphia: Lea and Febiger, 1952. $7.50.

This book, the first edition of which appeared in 1930, was universally welcomed by pathologists and physicians alike. It was a study of pathology of the living almost as much as of the dead, because of the inclusion of so much information regarding material obtained at operations upon diabetic patients. The second edition (1938) added 34 pages and was based upon 300 autopsies. Now, after fourteen years the third edition has appeared. During the interval the experience of the senior author has grown; his breadth of view has widened owing to his expanding work in pathology at the New England Deaconess and Baptist hospitals and Harvard Medical School, his supervision of diagnostic pathology for the State Tumor Diagnosis Service, his position as director of the Division of Biology and Medicine, United States Atomic Energy Commission, and finally, his directorship of the new Cancer Research Laboratory of the Deaconess Hospital. Through all these years Dr. Warren's interest in diabetes has continued; fortunately for the third edition, he has been joined in its preparation by Dr. Philip M. LeCompte, whose concern with the problem has been daily for eight years both at the Deaconess Hospital and later at the Faulkner Hospital, where, as pathologist, he had an unusual opportunity of studying the cases of pregnancy in young diabetic persons under the medical supervision of Dr. Priscilla White.

The source material of these authors is probably unequaled. It consists of over 800 autopsies as well as 50 autopsies on infants of diabetic mothers, in addition to the clinical material of the Deaconess Hospital, to which physicians interested in diabetes have brought their patients for half a century.

COLLEGE OF ... JAN ... STATE ... KANSAS

Such unrivaled data the authors have used wisely. With their presentation of facts they have interwoven discussions of the disease as it affects the kidneys, arteries and eyes. They have raised the possibility of harmonizing the lesions in various organs and tissues and thus of building up an explanation of what has been found in the glomeruli, in the eyes and elsewhere. The medicolegal aspects of diabetes have been considered in detail. New technics have been employed for the preparation of tissues and are described in detail.

It is safe to say that no pathological laboratory or clinic concerned with diabetes can fail to profit by this third edition, which combines discussions of the pathology of the disease with that of experimental research and then brings up broad conceptions for a new attack upon it.

ELLIOTT P. JOSLIN, M.D.

A Textbook of Orthopedics: With a section on neurology in orthopedics. By M. Beckett Howorth, M.D. 8°, cloth, 1110 pp., with 463 illustrations. Philadelphia: W. B. Saunders Company, 1952. $16.00.

Textbooks in medical specialties are of two types, small compendiums that give a panoramic view of the field, usually with no adequate description of the conditions relegated to that specialty, and large encyclopedic volumes that attempt to cover fully the entire field of the specialty. This book belongs to the latter class. Written with the assistance of 5 collaborators for special sections. it covers over 1100 pages. Orthopedic surgery has grown rapidly in the last half century, as this book shows, and continues to grow equally rapidly.

The book begins, appropriately, with a short chapter on the history of orthopedic surgery. In the latter part of this chapter the author does not recognize the many advances in therapy and in the public-health aspects of orthopedics introduced in other parts of the country than New York. The chapters on orthopedic examination and general orthopedic treatment, based on the author's many years of teaching, are excellent. They are the clearest exposition of general orthopedic principles appearing so far in any textbook. It is difficult to divide the diseases and disabilities treated by orthopedic surgery into regional conditions and general orthopedic disorders. It has been tried in several contemporary volumes but always with a certain amount of confusion. The author, having the example of the others as a guide, has made fewer mistakes, but this textbook still does not make a satisfactory division. Posture and its defects must be referred to the whole body and cannot be considered as a part of regional orthopedics. As the etiology and pathology of certain conditions have become clearer it has been easier to make a more logical and satisfactory classification of diseases. Such a classification has been achieved in this textbook. In keeping pace with present-day practice the author has added chapters describing a number of the "fringe" orthopedic diseases, particularly intoxications, certain types of trauma and neurological diseases. The book is written with care and scrupulous verification of data. The spirit of the conscientious teacher is on almost every page. Although the style is at times ponderous, the facts are presented clearly. Exception can sometimes be taken to the author's unvarying preference for the therapy of the Hibbs School. Prevention and prophylaxis are not slighted.

The illustrations, which have been selected with great care, are clear and specific. References added to each chapter give the original description of the lesion as well as the pertinent present-day medical literature. However, one can scarcely imagine how a busy student can find time to read the references after a perusal of the text. The format of the book is good.

This is probably the most complete and accurate textbook on orthopedic surgery that has yet been written. Several hundred pages, the chapters on anatomy and physiology, the chapter on fractures, except their complications, and much of the chapters on neurology could have been left out without hurting the book in any way. It is a more helpful volume for teachers than for students. It will prove to be an excellent reference work for all practitioner of orthopedic surgery.

JOHN G. KUHNS, M.D.

NONCLINICAL NOTES

GORGAS MEMORIAL AWARD

On November 19, at a meeting of the Association of Military Surgeons of the United States, which was addressed by the President of the United States, the Gorgas Memorial Award was given to Brigadier General James Stevens Simmons, U.S.A. (Ret.), dean of the Harvard School of Public Health.

The Gorgas Medal was established in 1942 by Wyeth, Incorporated, in memory of Surgeon General William Crawford Gorgas, whose work in preventive medicine made possible the construction of the Panama Canal.

APPOINTMENT OF DR. DAMMIN

Dr. Gustave J. Dammin, of St. Louis, has been appointed professor of pathology at Harvard Medical School and pathologist-in-chief of the Peter Bent Brigham Hospital, succeeding Dr. Clinton Van Zandt Hawn, who has resigned for reasons of health.

Dr. Dammin was formerly chairman of the Pathology Department of Washington University School of Medicine and pathologist-in-chief of the Barnes Hospital in St. Louis.

NOTICES

NEW YORK STATE HEALTH PUBLICATIONS EDITOR

A nationwide examination for health publications editor in the Department of Health, State of New York (annual salary, $6088–$7421), has been announced. This position in the Office of Public Health Education, under general supervision of the Director, is to direct the preparation of health education publications and periodicals.

Qualifications consist of a Bachelor's degree and three years of professional writing and editorial experience, including an aggregate of one year in the field of public health or medical science; and two more years of writing experience or one more year of professional writing experience and a Master's degree in journalism, English or public health. Additional information may be obtained from the Department of Civil Service, 39 Columbia Street, Albany, New York, or from Mr. Richard H. Mattox, Office of Personnel Administration, New York State Department of Health, State Office Building, Albany, New York.

Applications should be received by January 9, 1953.

SPRINGFIELD HOSPITAL EDUCATIONAL PROGRAM

The educational program of the Springfield Hospital for the month of January, 1953, is as follows:

Saturday, January 3
8:30–10:00 a.m. Surgical Service Conference, classroom, second floor.
10–11 a.m. Grand Surgical Rounds, Staff Conference Room.
11 a.m.–12 m. Combined Medical-Surgical Grand Rounds, Staff Conference Room.

Monday, January 5
6:30 p.m. Functional Diseases of the Thyroid Gland: Pathology and physiology. Staff Conference Room. Drs. William Kaufmann and Ahmad Nakib.

Friday, January 9
11 a.m.–12 m. Grand Medical Rounds, Staff Conference Room.
6:30 p.m. Diaphragmatic Hernias. Staff Conference Room. Dr. James W. S. Hartshorn, Jr.

Saturday, January 10
8:30–10:00 a.m. Surgical Service Conference, classroom, second floor.
10–11 a.m. Grand Surgical Rounds, Staff Conference Room.
11 a.m.–12 m. Clinicopathological Conference, Staff Conference Room.

Monday, January 12
6:30 p.m. Management of Emergencies in Chest Diseases. Staff Conference Room. Dr. James W. S. Hartshorn, Jr.

Friday, January 16
11 a.m.–12 m. Grand Medical Rounds. Staff Conference Room.
6:30 p.m. Breast Lesions. Staff Conference Room. Drs. William Kaufmann and Ahmad Nakib.

Saturday, January 17
8:30–10:00 a.m. Surgical Service Conference, classroom, second floor.
10–11 a.m. Grand Surgical Rounds, Staff Conference Room.
11 a.m.–12 m. Medical-Death Review, Staff Conference Room.

Monday, January 19
6:30 p.m. Basic Physiology of the Pancreas. Staff Conference Room. Dr. Peter S. Zarecki.

Tuesday, January 20
8:30 p.m. Guest Speaker Conference, Staff Conference Room, Dr. Frederick A. Post, bronchoscopist, Springfield Hospital, speaking on the subject "Carcinoma of the Esophagus."

Friday, January 23
11 a.m.–12 m. Grand Medical Rounds, Staff Conference Room.
6:30 p.m. Surgical Conditions of the Pancreas. Staff Conference Room. Dr. Peter S. Zarecki.

Saturday, January 24
8:30–10:00 a.m. Surgical Service Conference, classroom, second floor.
10–11 a.m. Grand Surgical Rounds, Staff Conference Room.
11 a.m.–12 m. Surgical-Death Review, Staff Conference Room.

Monday, January 26
6:30 p.m. Thoracolumbar Sympathectomy and Hypertensive Disease. Staff Conference Room. Dr. Field C. Leonard.

Friday, January 30
11 a.m.–12 m. Grand Medical Rounds, Staff Conference Room.
6:30 p.m. Proper Use of Parenteral Fluids As Supportive Therapy. Staff Conference Room. Dr. Ahmad Nakib.

Saturday, January 31
8:30–10:00 a.m. Surgical Service Conference, classroom, second floor.
10–11 a.m. Grand Surgical Rounds, Staff Conference Room.
11 a.m.–12 m. Radiology Conference, Staff Conference Room. Dr. Robert A. Grugan.

Every Wednesday, from 11 a.m. to 12 noon, a psychosomatic and group-psychotherapy conference is held in the Staff Room under the direction of Dr. Calvert Stein. Every Thursday, from 3 to 4 p.m., a pathology conference is held in the Staff Conference Room.

NEW ENGLAND CARDIOVASCULAR SOCIETY

A meeting of the New England Cardiovascular Society will be presented by the Peter Bent Brigham Hospital, with invited papers from New England, on Monday, January 5, 1953, at 8 p.m. at the Dorothy Quincy Suite of John Hancock Hall, 180 Berkeley Street, Boston.

PROGRAM

Peter Bent Brigham Hospital, Samuel A. Levine, M.D., presiding:

Experimental and Clinical Aspects of Paroxysmal Auricular Tachycardia with Block. Harold D. Levine, M.D., Norman F. Wyatt, M.D., and Bernard Lown, M.D.

Cor Pulmonale. Lewis Dexter, M.D., Florence W. Haynes, Ph.D., Lawson McDonald, M.D., Murray Rabinovitz, M.D., and George Saxton, Jr., M.D.

A Digitalis-Tolerance Test. Bernard Lown, M.D., Augustus T. Crocker, M.D., and Samuel A. Levine, M.D.

Invited Papers from New England, C. Sidney Burwell, M.D., presiding:

Studies of Stress: Interrelation of Emotional Responses and Cardioballistographic Tracings. Daniel H. Funkenstein, M.D., and Stanley King, M.A.

Acute Pericarditis Complicating Infectious Mononucleosis. Henry Miller, M.D., J. Urrichio, M.D., and R. Phillips, M.D.

The Duration of the QU Interval of the Electrocardiogram and Its Components in Hypopotassemia with and without Hypocalcemia. Eugene Lepeschkin, M.D., and Borys Surawicz, M.D.

Interested physicians, medical students and members of the New England Postgraduate Assembly are cordially invited to attend.

Free parking privileges are available on St. James Avenue above Clarendon Street. No attendant is on duty. Emergency telephone numbers are Devonshire 8-9081 and Devonshire 8-9296.

FIRST WORLD CONGRESS ON FERTILITY AND STERILITY

The First World Congress on Fertility and Sterility will be held at the Henry Hudson Hotel, New York City, May 25-31, 1953, under the joint sponsorship of the International Fertility Association and the American Society for the Study of Sterility.

Twenty-three scientific sessions will embrace the entire field of fertility and sterility, including sessions dealing with socioeconomic factors, psychosomatic aspects and artificial insemination. The sessions will be conducted in English, French and Spanish, with the use of earphones and simultaneous translations, as in the United Nations meetings.

In addition to the scientific sessions there will be medical round-table discussions, question-and-answer periods, scientific exhibits and motion pictures.

Since seats will be at a premium, it is suggested that those who plan to attend write as soon as possible to the Chairman of the Local Arrangements Committee, 1160 Fifth Avenue, New York 29, New York, for advance registration.

AMERICAN COLLEGE OF RADIOLOGY

The annual meeting of the American College of Radiology will be held at the Palmer House, Chicago, on February 6, 1953. In addition to the councilors' luncheon and annual banquet, the program will include election of officers and committee reports.

The Gold Medal of the College will be awarded to Dr. Arthur C. Christie, of Washington, D. C., and Dr. Edward H. Skinner, of Kansas City, Missouri.

SPRINGFIELD ACADEMY OF MEDICINE

A regular meeting of the Springfield Academy of Medicine will be held on January 13, 1953. Dr. J. Roswell Gallagher, chief of the Adolescent Unit at the Children's Medical Center, Boston, and assistant professor of child health, Harvard School of Public Health, will speak on the subject "Office Handling of the Adolescent."

DEFERMENT OF PRIORITY III PHYSICIANS TO SERVE AS HOSPITAL RESIDENTS

The National Advisory Committee to the Selective Service System announces that when the supply of Priority I and Priority II physicians is exhausted, as will occur in the near future, the only source of physicians available for service as junior medical officers will be recent medical graduates who are obligated for military service under the basic Selective Service law and other medical graduates who are in Priority III under the provisions of Public Law 779. That this group may be available for service before older Priority III physicians are called, the National Advisory Committee recommends that, until further notice, medical graduates be considered available for military service immediately upon completion of one year of internship and not be recommended

for deferment for residency training. Hospitals should fill their residencies first from medical graduates who already have had military service — a group that constitutes almost 80 per cent of current interns; secondly, from physicians who are being discharged from service, the number of whom now equals the number of physicians being called to active duty; and finally from women and other physicians who are not obligated for military service.

The National Advisory Committee also recommends that hospital residents registered under the basic Selective Service law and those in Priority III under Public Law 779 be released when called by Selective Service and replaced by physicians from the groups suggested above. Special consideration should be given to those who have only a few months to complete their training. These must be considered on an individual basis, with due regard for both the individual and the institution.

FELLOWSHIPS IN INDUSTRIAL MEDICINE

Eight fellowships in industrial medicine will be offered by the United States Atomic Energy Commission for the 1953–54 academic year. The fellowship program is designed to provide advanced training and on-the-job experience for men and women physicians in the field of industrial medicine, particularly in relation to the atomic energy industry.

The fellowships are open to United States citizens who hold M.D. degrees from approved medical schools, and who have had at least one year of internship. In exceptional cases, equivalent experience may be accepted in lieu of the internship requirement. Successful candidates must be investigated by the Federal Bureau of Investigation and approved by the AEC before receiving fellowships.

Awards are for one year's academic training at institutions offering approved graduate courses in industrial medicine that can provide special training facilities in the health problems associated with the atomic-energy program. Normally, fellows will be eligible for a second, or in-plant, training year in medical departments of major AEC plants and laboratories upon successful completion of the academic year.

There is a critical need for qualified industrial physicians in atomic-energy installations, and at the end of the two-year training period fellows may find employment in the program. However, there will be no commitment on the part of the AEC to continue the applicant's training beyond first year or to provide employment for him upon the completion of training. Fellows will not be obligated to take the second year of training or to seek employment with the AEC or its contractors.

The stipend during the first year is $3,600, with $350 additional for a wife and for each dependent child. Tuition and laboratory fees will be paid. The stipend for the second year is $6,000, with no additional amounts for a wife or children.

The program is administered for the AEC by the Atomic Energy Project of the School of Medicine and Dentistry, University of Rochester, Rochester, New York. Fellows are selected by a committee headed by Dr. A. G. Kammer professor of occupational health, Graduate School of Public Health, University of Pittsburgh, and medical director of the Carbide and Carbon Chemicals Company.

Applications for 1953–54 fellowships should be submitted by January 1, 1953 to AEC Fellowships in Industrial Medicine, Atomic Energy Project, University of Rochester School of Medicine and Dentistry, Rochester, New York (Attention: Dr. Henry A. Blair).

SOCIETY MEETINGS AND CONFERENCES

DECEMBER 18. New England Pathological Society. Page 958, issue of December 11.

DECEMBER 19–22. Springfield Hospital Educational Program. Page 827, issue of November 20.

DECEMBER 19–JANUARY 30. Combined Anesthesia Teaching Conferences of Boston. Page 785, issue of November 13.

DECEMBER 29–MARCH 23. Postgraduate Course in General Medicine. Page 697, issue of October 30.

JANUARY 3–31. Springfield Hospital Educational Program. Page 1000.

JANUARY 3–JUNE 2. Mount Auburn Hospital Panel Discussions. Page 868, issue of November 27.

JANUARY 5. New England Cardiovascular Society. Page 1001.

JANUARY 7–APRIL 8. Postgraduate Medical Institute. Page 452, issue of September 18.

JANUARY 13. Springfield Academy of Medicine. Page 1001.

JANUARY 14. Essex North District Medical Society. Page 743, issue of November 6.

FEBRUARY 6. New England Society of Anesthesiologists. Page 827, issue of November 20.

FEBRUARY 6. American College of Radiology. Page 1001.

FEBRUARY 9 AND 10. Annual Congress on Medical Education and Licensure. Page 786, issue of November 13.

MARCH 2–5. New Orleans Graduate Medical Assembly. Page 828, issue of November 20.

MARCH 2–MAY 4. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 540, issue of October 2.

APRIL 3. New England Society of Anesthesiologists. Page 418, issue of September 11.

APRIL 29 AND OCTOBER 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.

MAY 25–31. First World Congress on Fertility and Sterility. Page 1001.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 14. Pentucket Club. 111 Main Street, Haverhill.

MAY 13. Andover Country Club, Shawsheen.

MIDDLESEX WEST

DECEMBER 29–MARCH 25. Postgraduate Course in General Medicine.

NORFOLK

JANUARY 27.

FEBRUARY 24.

MARCH 24.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, DECEMBER 25

FRIDAY, DECEMBER 26

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit. 57 East Concord Street.

*10:00 a.m.–1:00 p.m. Medical and Surgical Grand Rounds. Dr. George W. Thorn and Dr. Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.

10:30–11:15 a.m. Diabetes Lecture. Dr. Elliott Joslin. New England Deaconess Hospital.

11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.

*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.

4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

*7:00–9:00 p.m. Combined Anesthesia Teaching Conferences of Boston. Amphitheater, Evans Memorial, Massachusetts Memorial Hospitals, Eighth Floor, 65 East Newton Street.

SATURDAY, DECEMBER 27

*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.

*9:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.

*11:00 a.m.–12:00 m. Blood Clinic. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, DECEMBER 29

*8:00–9:00 a.m. Combined Medical and Surgical Rounds for Diabetic Surgery Cases. New England Deaconess Hospital.

*8:30–9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

5:15 p.m. Staff Meeting. Harris Hall, New England Deaconess Hospital.

*7:00–9:00 p.m. Anesthesia Teaching Conference. Stearns Auditorium, New England Center Hospital.

TUESDAY, DECEMBER 30

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.

*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.

*5:00–6:00 p.m. Service Meeting followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.

WEDNESDAY, DECEMBER 31

*12:00 m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.

12:30 p.m. Weekly Pathological Meeting. Joslin Amphitheater, New England Deaconess Hospital.

*4:00 p.m. Thoracic Conference. Held by Overholt Clinic. Harris Hall, New England Deaconess Hospital.

*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.

*Open to the medical profession.